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ARCHIVES OF SURGERY

VOLUME 20 MARCH, 1930 NUMBER 3

THE RESORPTION OF BONE

A CONSIDERATION OF THE UNDERLYING PROCESSES PARTICULARLY IN PATHOLOGIC CONDITIONS *

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The earliest workers in bone were concerned with its resorption. Howship,[1] in 1815 and 1817, discussed physiologic and pathologic resorption, but others before him had already called attention to this subject. Later, Koelliker,[2] using the newer methods of histologic technic, applied himself especially to a study of physiologic resorption and recognized the importance in this process of the multinucleated giant cell, which he called osteoclast (bone breaker). Many of his conclusions in regard to the osteoclast have been applied in their entirety to patholigic resorption, with the consequent neglect of other factors which play a part in such resorption. Even physiologic resorption is not brought about solely by osteoclasts.

Physiologic resorption was recognized many decades ago as important in the development of the skeleton, which is reconstructed several times before it reaches its adult form. Physiologic resorption can be studied when the cartilaginous skeleton is removed and replaced by the coarse-fibered bone of the primary skeleton. Later, the primary bone is resorbed and replaced by lamellar bone.[3] That constant physiologic resorption goes on in lamellar bone was recognized long ago, but the physiologic and chemical importance of this reconstruction has recently been brought into relief, as it has been bound up with the subject of mineral metabolism.

In this paper, I shall deal chiefly with the subject of pathologic resorption. It is sometimes difficult to draw the line between physiologic

* Submitted for publication, Sept. 3, 1929.

1. Howship, J.: Experiments and Observations in Order to Ascertain the Means Employed by the Animal Economy in the Formation of Bone, Med.-Chir. Tr. **6**:263, 1815; Observations on the Morbid Structure of Bones and Attempt at an Arrangement of Their Diseases, ibid. **8**:57, 1817.

2. Koelliker, A.: Die normale Resorption des Knochengewebes, Leipzig, F. C. W. Vogel, 1873.

3. Jaffe, H. L.: The Structure of Bone, with Particular Reference to Its Fibrillar Nature and the Relation of Function to Internal Architecture, Arch. Surg. **19**:24 (July) 1929.

and pathologic resorption. For instance, should old age osteoporosis and inactivity osteoporosis be classed under physiologic or pathologic resorption? In a discussion of resorption of bone in general, such as this is, it is not necessary to make such distinctions. The resorption varies with the individual conditions that are producing it, but I do not plan to discuss in detail how these resorptive processes vary in specific diseases. Pathologic resorption is seen in acute and chronic inflammatory diseases of bone; it occurs in all localized resorptive processes in connection with tumors and aneurysms; in metabolic bone disease resorption is often prominent; in the reconstruction of callus and transplants and in the dissolution of callus and sequestrums various degrees of resorption are seen.

I shall aim to give a balanced conception of pathologic resorption. A survey of the literature shows that previous discussions have frequently been limited to one phase of the problem, resulting in its overemphasis. The conclusions drawn concerning the pathogenesis of pathologic resorption must be interpreted with regard to the material used in the investigation. The development of resorption brought about by the ingestion of acids or acid salts will differ in several ways from that due to starvation, and the process of resorption in these two will be different from the resorption of bone in acute inflammatory diseases. In addition to the basic etiologic factor, the resorptive picture is influenced by the severity and acuteness of the process.

Resorption may be accomplished by osteoclasts or by blood vessels and granulation tissue. There has been much controversy as to whether or not a preliminary decalcification of the bone is necessary before there can be resorption by osteoclasts and blood vessels. The importance attached to the part which the lacunae and canaliculi of the bone cells play in resorption has varied considerably. There has been a tendency to attach too much importance to the resorption of bone by osteoclasts. Osteoclastic resorption plays rather an insignificant part in the more fulminating inflammatory bone diseases.

Vascular resorption, mentioned in 1793 by Weidmann [4] and in 1817 by Howship, was first described as a widening of the existing vessel canals. Attention was again focused on it when descriptions of newly formed vascular spaces in resorbing bone were published by Tomes and de Morgan [5] in 1853, and subsequently independently described by Volkmann [6] in 1863. These newly formed vessel canals of bone are now known as Volkmann's canals. The increased vascularization of

4. Weidmann, J. P.: Ueber den Brand der Knochen, Frankfurt, A. M. Andreas, 1793; German translation, Leipzig, 1797.

5. Tomes, J., and de Morgan, C.: Observations on the Structure and Development of Bone, Phil. Tr., Lond. **143**:109, 1853.

6. Volkmann, R.: Zur Histologie der Caries und Ostitis, Arch. f. klin. Chir. **4**:436, 1863.

the marrow, the enlargement of the existing vessel canals and the perforation of both the compact and the spongy bone by newly formed vessels, extending out from the preexisting vessels, rapidly reduce the amount of bony tissue.

Howship, in discussing vascular resorption, described the enlargement of the haversian canals, the surfaces of which either remained smooth or exhibited a rough and uneven appearance. The uneven, irregular depressions in the walls of the haversian canals, to which Howship called attention, are now known as Howship's lacunae, the name having been extended to apply to all depressions produced beneath the periosteum or endosteum, on the walls of the canals, or on the surfaces of the spongy trabeculae during the course of the resorption of bone.

Following Virchow,[7] who attached much significance to the degeneration of the bone cell and its surrounding bone (cell territories) in resorption and in the formation of Howship's lacunae, were many who advocated his theory and who even modified it to account for the origin of Volkmann's canals from enlarged lacunae and canaliculi of bone cells. These views were assailed by those who ascribed to the osteoclasts the sole and exclusive ability to form Howship's lacunae, and by those who viewed Volkmann's canals as newly formed vessel canals of bone. But there may be some truth in what Virchow and his followers described particularly in regard to the formation of lacunae by local bone cell and matrix degeneration. Vascular resorption can also produce such lacunae in bone.

When pathologic resorption occurs, I believe that the histologic picture is a composite one, owing to the superposition of the pictures produced by the various cellular, vascular and chemical influences exerted on the bone. The resorptive picture in each case is determined by the stimulus to resorption and other factors, such as the particular bone in which resorption is taking place, the age of the subject and the state of nutrition.

This paper is based on a study of the literature of resorption in general, as well as on experience with a large amount of material from this laboratory, illustrating the resorptive processes in bone. The material includes embryonal bones, bone transplants, experimental osteoporosis, acute and chronic inflammatory diseases and bone tumors. The material was studied in a variety of ways. The sections were decalcified in Müller's solution, Müller plus 5 per cent glacial acetic acid, 5 per cent nitric acid or von Ebner's solution. Frozen or paraffin sections were cut and some ground disks were made by the file method, using bone fixed in formaldehyde. The sections were studied either unstained or stained by the following methods: Mallory's eosin and

7. Virchow, R.: Die Cellularpathologie, Berlin, A. Hirschwald, 1871, vol. 1.

methylene blue (methylthionine chloride, U. S. P.) hematoxylin and eosin, Mallory's connective tissue stain, or Foot's modification of the Bielschowsky-Maresch silver impregnation technic. Most of the methods used have been described in another paper.[8]

VASCULAR RESORPTION

By vascular resorption is meant the disappearance of bone through the agency of blood vessels and granulation tissue, resulting in enlargement of the existing vessel canals, the appearance of newly formed vessel canals and changes in the marrow.

The Vessel Canals of Normal Bone.—To understand vascular resorption a conception of the extent and ramification of the normal vascular channels, both in the bone and in the marrow, is necessary If a tubular bone is examined, it will be noted that blood vessels are carried through the compact bone by a series of vessel canals which anastomose and communicate with each other, and which convey the blood from the periosteum to the marrow cavity. The surfaces of the spongy trabeculae are for the most part nourished by the vessels of the marrow, but some of the larger spongy trabeculae may contain vessel canals. In adult bone cortex, the system of canals consists of the haversian canals, which run for the most part longitudinally, and the canals of the ground lamellae which run either circumferentially in the ground lamellae or transversely through them. A system of communicating canals connects the haversian canals with each other and like the haversian canals and the canals of the ground lamellae was formed by the deposition of bone around preformed vessels. A typical haversian canal usually contains at least two capillary vessels and some connective tissue. The larger ones may contain fat and lymphoid marrow.

The vessels canals of the cortex, as seen in a longitudinal section, appear as a continuous anastomosing and ramifying network beneath the articular cartilage at the upper or lower end of a bone, a longitudinal section discloses a number of haversian canals in cross-section, which means that in this region the haversian canals have changed their direction and run transversely to the long diameter of the bone. Some of the larger spongy trabeculae contain haversian canals that run transversely to the long axis of the bone. The canals of the spongy trabeculae connect with the marrow spaces by means of short, narrow communicating canals which are cut through their long axes in a longitudinal section of the bone.

The canals of the external ground lamellae are a means of connecting the vessels in the haversian canals with the periosteal vessels, and

8. Jaffe, H. L.: Methods for the Histologic Study of Normal and Diseased Bone, Arch. Path. **8**:817 (Nov.) 1929.

the vessels in the haversian canals are connected with the marrow cavity by means of the vessels in the canals of the internal ground lamellae (figs. 1, 2 and 3). In another paper, I described in detail the vessel canals of normal and pathologic bone.[9]

Changes in the Vessel Canals During Resorption.—In resorption of bone, particularly in the more fulminating and inflammatory diseases, enlargement of all the existing canals is well demonstrated in the cortex and a dilatation and increase in the number of blood vessels contained within them. The vascular dilatation is similar to the dilatation of

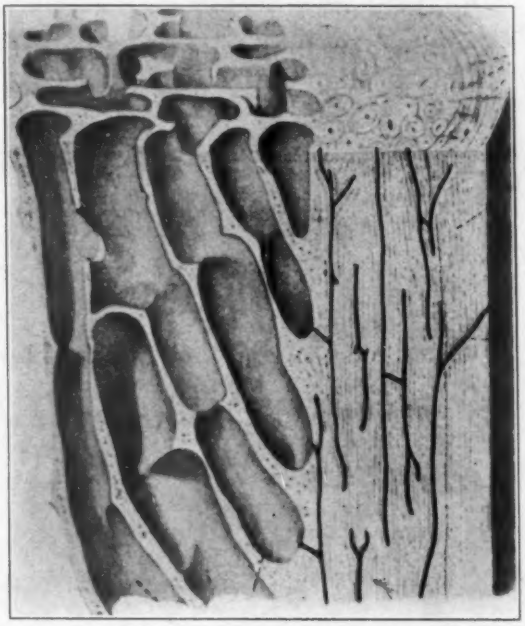

Fig. 1.—Diagrammatic representation of a longitudinal view of a bone, showing both compacta and spongiosa. The cortex on the right shows the outer ground lamellae, with some Sharpey fibers penetrating them. The haversian systems are illustrated, and the longitudinally directed haversian canals connected by the communicating canals are shown after Braus.

smaller blood vessels everywhere in the body in the course of inflammation, and the increased number of vessels results from the proliferation of the vessels already present. Concomitantly with this increased vascularization, an enlargement of the caliber of the vessel canals occurs. If the diaphyseal portion of the compacta from a case of progressive chronic osteomyelitis is examined in cross-section, it is found to contain

9. Jaffe, H. L.: The Vessel Canals in Normal and Pathological Bone, Am. J. Path. **5**:323, 1929.

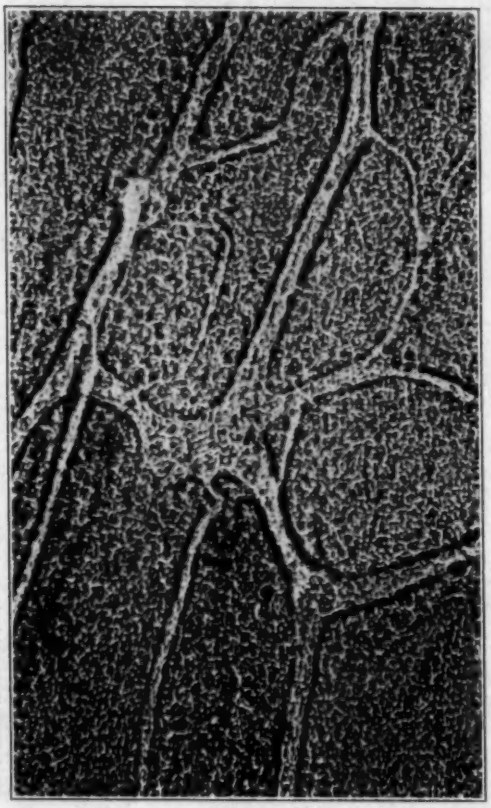

Fig. 2.—Longitudinal section of normal cortical bone, showing the anastomosing and branching haversian canals. The communicating canals between the haversian canals are demonstrated. The regularity and smoothness of the walls and the narrow lumina of the canals are to be noted. Unstained ground disk; × 75.

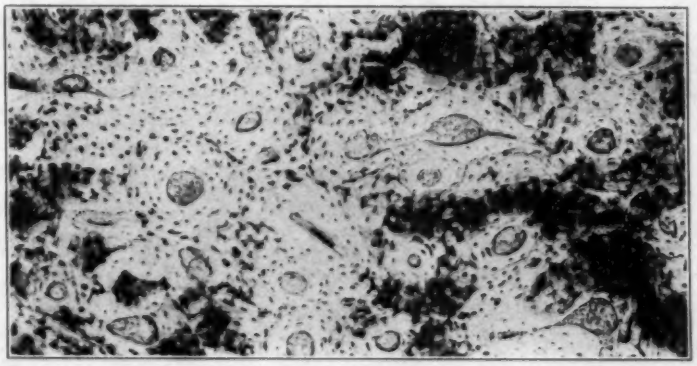

Fig. 3.—Part of a cross-section of the normal cortex, showing the haversian canals, and in the upper portion of the picture an haversian canal anastomosing with two adjacent haversian canals by means of communicating canals. Note the small diameters of the canals. Unstained ground disk; × 75.

haversian canals, the diameters of which are increased from one to several times. All haversian canals are not uniformly enlarged. Depending more or less directly on the severity of the process, few or many might not be enlarged at all. In cross-section it will also be seen, and this is more common in the severer inflammatory processes, that there is an actual coalescence or tendency to coalesce of several of the enlarged haversian canals, the thin bony partitions between them disappearing completely and resulting in the formation of large spaces in the bone, containing numerous blood vessels and considerable vascular granulation tissue. The enlargement of the canals is not limited to the haversian

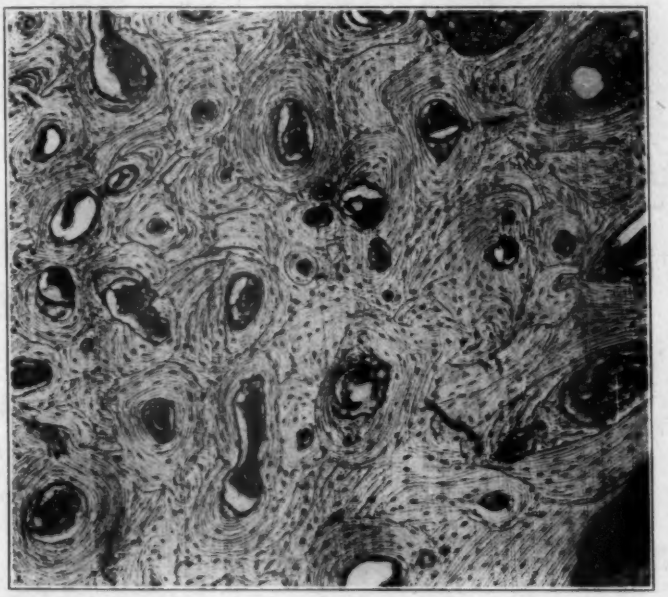

Fig. 4.—Cross-section of the compacta from a case of chronic osteomyelitis. Many of the haversian canals are much enlarged and filled with granulation tissue. The walls are smooth. An enlarged communicating canal is seen. Frozen section stained with gallein; × 75. Compare with figure 3.

canals, but all the canals of the cortex are subject to the same process of enlargement, this being true also of the few canals of the spongy trabeculae (figs. 4 and 5).

The enlargement of the existing canals may be in the nature of a uniform enlargement of their caliber, the walls of the canals remaining smooth, or it may be associated with the appearance of indentations on the walls of the canal at various levels. These indentations correspond to those frequenly seen on the surfaces of the spongy trabeculae, and are known as Howship's lacunae (fig. 6). Such lacunae are not so frequent on the walls of the vessel canals as they are on the spongy

trabeculae, and this is probably due to the fact that the spongy trabeculae are more exposed to granulation tissue in inflammatory processes.

The extent and the course of the canals are also changed during vascular resorption. While the haversian canals usually run longitudinally, in inflamed bone their course becomes tortuous and is lengthened. A longitudinal section of inflamed compact bone will show cross-sections of haversian canals, owing to the fact that these canals, because of their tortuosity, have been cut through a turn in the canal.

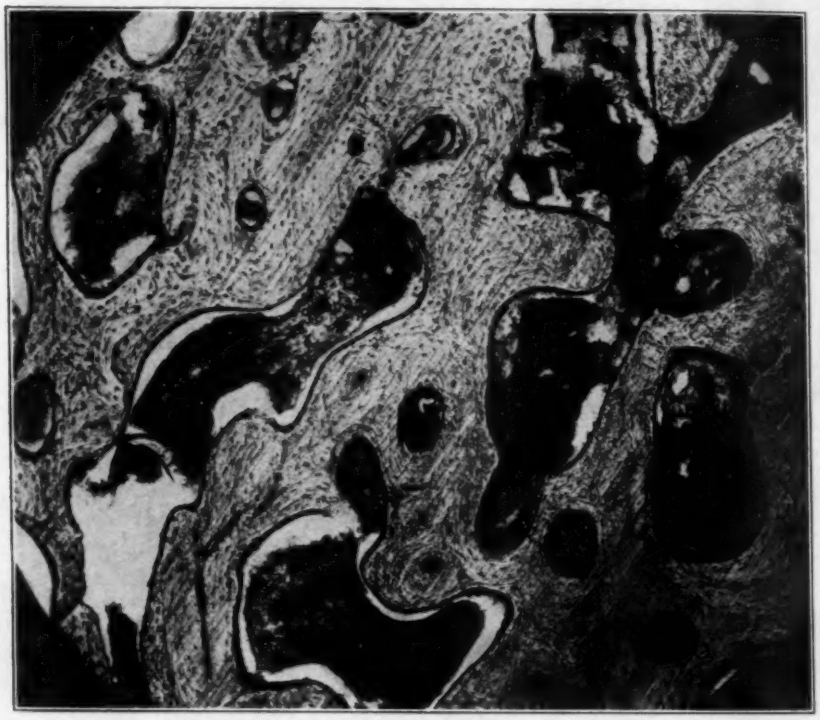

Fig. 5.—Cross-section of the compacta from a case of chronic osteomyelitis, showing the spaces formed by the coalescence of extremely enlarged haversian canals. A few haversian canals are still not enlarged. The sinus-like spaces are filled with vessels and granulation tissue. The walls of the spaces are smooth. The spaces extend irregularly through the compacta. Frozen section stained with gallein; × 75.

New Canals in Resorbing Bone.—Volkmann, in 1863, described the appearance of numerous newly formed vessel canals in the cortex of diseased bone, which differed from the existing canals in size, arrangement and vessel content. These canals had irregular, toothed borders and were narrow, but of varying caliber. They were not surrounded by concentric lamellae, but broke through the lamellae surrounding the

existing blood vessels. Their course was irregular, and sometimes they extended snake-like through the entire thickness of the cortex. These canals have come to be known as Volkmann's canals. In its earliest form, a Volkmann canal appears as a short, irregular, fine crack in the ground substance, radiating from a haversian canal, from which several of them may be seen coming off. As the canal grows, a branch or

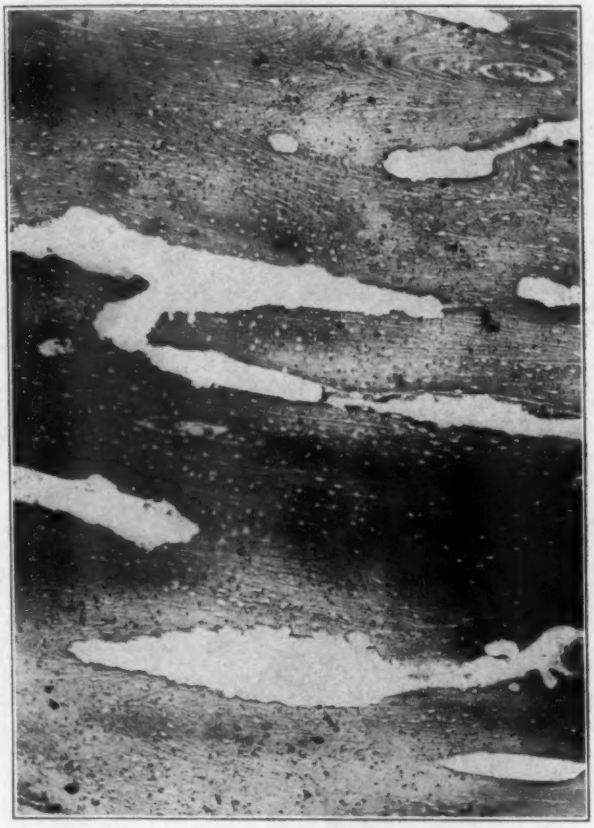

Fig. 6.—Longitudinal section of the cortex from a case of osteomyelitis. The haversian canals are enlarged in diameter, and the walls are irregularly indented, showing Howship's lacunae. Compare with figure 2. Frozen section stained with Bielschowsky's silver stain; × 75.

branches from the haversian vessel vascularize it. In vascular resorption of bone, the enlargement of the existing vessel canals is more important in reducing the bone substance than the formation of Volkmann's canals (figs. 7, 8, 9 and 10).

Changes in the Marrow During Vascular Resorption.—While these changes are taking place in the cortex, the character of the marrow is

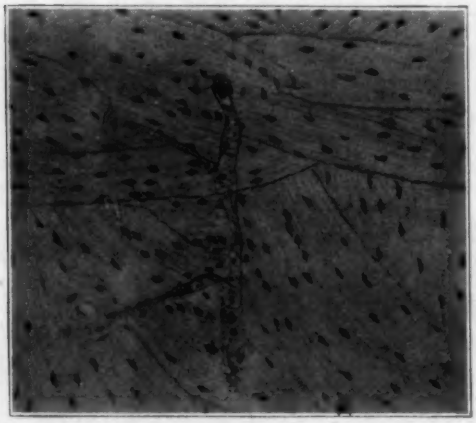

Fig. 7.—Camera lucida drawing showing the development of three newly formed passages. The larger, vertical one extends from a haversian canal above to one below. Below a fine triangular passage is seen extending through the interstitial and haversian lamellae as it approaches an haversian canal. Some of the characteristics of Volkmann canals are shown. Magnification about 100.

Fig. 8.—High power camera lucida drawing, showing the details of a crack in the ground substance that will become a Volkmann canal. The crack breaks through the lamellae, including the cement lines, passing directly through the bone cell lacunae that lie in its path. Coarse granules of decalcified material are contained within the crack, along with some nuclear débris. Note the irregular walls of the crack. Magnification about 600.

also altered. Normally the vessels of the marrow are derived from the nutrient artery, which enters the diaphysis through the nutrient canal, and from the numerous metaphyseal and epiphyseal vessels which enter the medullary cavity through the thin cortex in the respective regions. The general pattern of the arterial vascular system of bone-marrow has long been known. It is made up of the nutrient artery which divides on entering the marrow cavity, and which gives off one branch

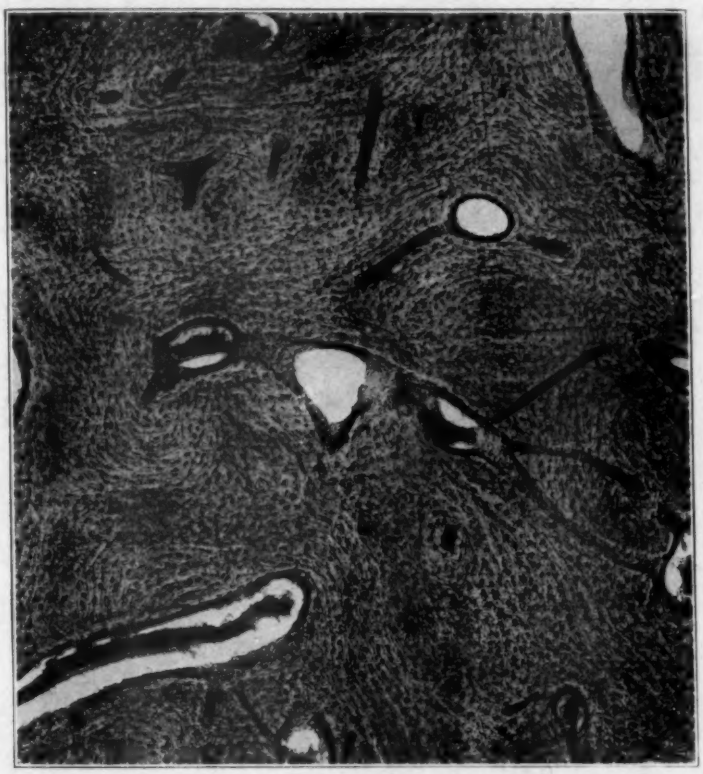

Fig. 9.—Section of bone cortex, showing some enlarged haversian canals and numerous newly formed Volkmann canals criss-crossing through the ground substance. Frozen section, stained with gallein; × 75.

which passes to each epiphysis. These main branches give off finer branches. In the region of the metaphysis and epiphysis, numerous nourishing vessels penetrate the cortex of the bone to enter the marrow cavity. While the compact bone receives nearly all its vessels from the periosteum, the nutrient, metaphyseal and epiphyseal vessels on passing through the compact bone also supply some branches to the bone cortex. These branches anastomose within the cortex with vessels that entered from the periosteum. The vessels of the cortex nearest

the medullary cavity anastomose with the marrow vessels. There is, therefore, an extensive anastomotic connection within the cortex between the vessels of the periosteum, and the epiphyseal, metaphyseal and nutrient artery branches, while within the medullary cavity branches of the latter three vessels anastomose with those of the periosteum that have entered after passing through the cortex.

Fig. 10.—Cross-section of human adult cortical bone from a case of osteomyelitis, showing enlarged haversian canals, giving rise to several transverse, newly formed, perforating canals of Volkmann. Some of the Volkmann canals join other haversian canals.

Because of this intimate anastomotic connection, changes that affect the cortex also leave their mark on the marrow. In a severe inflammatory process, the marrow becomes extremely vascularized, as a result of the proliferation of the existing vessels. The newly formed vessels appear as dilated congested channels. Connective tissue also increases;

the lymphoid marrow disappears and is replaced by polymorphonuclear leukocytes with a sprinkling of inflammatory exudative cells in the severer lesions. In the less severe lesions more fibroblastic proliferation is present and greater numbers of lymphocytes, plasma cells, eosinophils and inflammatory exudative cells appear. As a result, there is encroachment of vessels and granulation tissue on the marrow surface of the cortex and on the surfaces of spongy trabeculae which become thinner and smaller and which may appear gouged out owing to the development of numerous depressions which are the Howship's lacunae (fig. 11). The speed of the destruction of the spongy trabeculae is dependent on

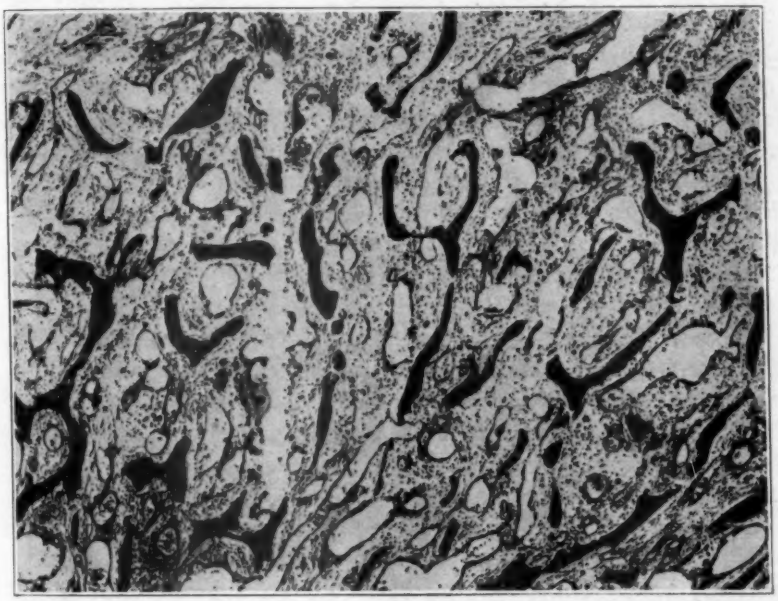

Fig. 11.—Section through the rib of a dog suffering from experimental osteoporosis due to calcium deficiency. It shows the atrophic spongy trabeculae, disappearance of the lymphoid marrow which is replaced by a loose connective tissue containing numerous blood vessels, many of which are in apposition with the atrophic spongy trabeculae. Paraffin section stained by Bielschowsky-Maresch silver stain; × 75.

the severity of the lesion. In the severer lesions, the spongy trabeculae seem to be resorbed without osteoclasts. The resorption of the spongy trabeculae must be viewed as analogous to the enlargement of the vessel canals of the cortex. Because of the thinness of the trabeculae and the greater vascularity of the surrounding tissue, they are more vulnerable to resorption.

The spongy trabeculae may also be penetrated by newly formed vessel canals and those canals already present may become enlarged,

similarly to those in the cortex. During resorption, the osteoblasts lining the trabeculae and the various canals disappear, and new bone formation ceases. The osteoblasts do not reappear until degeneration takes place. Sometimes in the same section certain areas show resorption still in progress and an adjacent area may show cessation of resorption or the resumption of degeneration. The same trabecula may show resorption on one surface and bone regeneration on the other.

The Mechanism of Vascular Resorption.—In discussing vascular resorption, I described the changes as they occur when the resorption is acute and extensive. I indicated that the vascular changes in resorption vary with the severity and the cause of the resorption. While vascular factors are associated with the resorption of bone during old age, the changes are not so radical as they are in even a mild inflammatory process, but they are present. There are differences in the character of the vascular changes of resorption in the various inflammatory diseases of bone, which is also true in regard to the resorption caused by varying degrees of calcium deficiency in the diet. The amount of dilatation of the vessel canals depends more or less on the degree of vascularization, the speed and extent of the resorption being less when fewer vessels are present and when the granulation tissue is more cellular.

The question as to how vascular resorption occurs arises. There is no doubt that osteoclasts play little or no part here. In fact, they are rather infrequently seen on the walls of the vessel canals in the more acute resorptive conditions and they seldom appear on the trabeculae in such conditions.

Whether enlargement of the vessel canals and the formation of Volkmann's canals are preceded by a decalcification of the bone has not been decided. It is difficult to conceive that the extensive enlargement of the existing vessel canals and the formation of new vessel canals, taking place at the rate they do under many conditions, should not be preceded by or simultaneously associated with decalcification of the bone ground substance in the vicinity of the vessels. Normally the condition of calcium equilibrium in the adult is undoubtedly an instance of dynamic equilibrium in which the decalcification that is constantly going on is balanced almost exactly by calcification which is also a continuous process. Normally the calcium ingested in food replaces the calcium lost from the bone in the normal process of bone metabolism. The calcium excreted represents, therefore, the excess of calcium ingested plus the calcium lost from the bone. In an adult animal in which calcium equilibrium has been attained, the amount ingested equals the amount excreted almost exactly. It must be understood, however, that the calcium equilibrium may be disturbed by the ingestion of certain electrolytes that may displace calcium from the bone or may so change

the composition of the circulating fluids as to favor the excessive solution of calcium from the bone. Should calcium be withdrawn from the diet, then a negative calcium balance would also develop and conceivably the bone in the vicinity of the vessels would become relatively decalcified. The remaining organic ground substance is then more susceptible to enzymic or cellular influences favoring its removal.

For obtaining histologic evidence of decalcification, only the ground disk methods are useful. Ground disks of bone fixed in formaldehyde show that enlargement of the vessel canals is accompanied by changes in the ground substance of the bone, particularly in the calcium salts which, in the region of the resorption, appear as large, irregular, coarse granules. In ground disks of normal bone they appear as fine, regular granules.

The way in which the bone becomes decalcified and what part the vessels and granulation tissue that have invaded the vessel canals play are still matters of speculation. The direct ability of the endothelial cells of the blood vessels to resorb the bone has been advocated by many and recently particularly by Pommer,[10] but others have denied this. The way in which the ground substance is decalcified depends on the cause of the bone resorption.

That bone may be decalcified in vivo has been shown by the fact that dietary deficiencies may lead to its decalcification. Experimental osteoporosis due to calcium deficiency is a well known example. Bone may be quickly decalcified in vivo by the administration of acids or acid salts, while starvation will also lead to similar results. Histologic evidence of decalcification in these instances is supported by chemical analysis of the bone. These facts are recited to show that in certain conditions of bone resorption decalcification is present and apparently precedes the enlargement of the vessel canals by a variable time interval. The results obtained from a study of the chemical and dietary deficiencies of bone are to some degree applicable to a study of the resorption due to inflammatory diseases, bone tumors, etc. It seems that the resorption of bone under any condition is dependent on previous decalcification. In inflammatory diseases the increased blood flow to the bone may be associated with local changes in the hydrogen ion concentration. The blood plasma and lymph are so well buffered that changes in hydrogen ion concentration are not easily produced. Cellular metabolism, however, occurs under conditions which suggest that different p_H concentrations may exist in different portions of the same cell. The recent work of Chambers with his microdissection technic has shown this. These changes may even be more extensive without being reflected in a lower plasma p_H. Such increased local acidity may result in the

10. Pommer, G.: Ueber Osteoporose, ihren Ursprung und ihre differentialdiagnostische Bedeutung, Arch. f. klin. Chir. **136**:1, 1925.

production of narrow zones of either complete or relative decalcification in the vicinity of the vessels. These narrow zones of decalcified organic matrix permit further enlargement of the vessel canals when they are removed. As the vessel canals enlarge, newly formed vessels and granulation tissue appear in them. The decalcified organic matrix is removed by tissue enzymes or by phagocytes in the granulation tissue. Just how this change in the p_H is made is not known. It may be due to local disturbances in the carbon dioxide tension, to local lactic acid production or locally to deficient oxidation.

I have indicated that decalcification may be brought about by a number of agents, both local and general. The extent of the preliminary decalcification depends on the cause of the decalcification. Decalcification due to ingestion of acids or acid salts or calcium deprivation may be of much greater extent than the decalcification due to local inflammatory conditions. The slow removal of the decalcified organic matrix accounts for the histologic evidences of calcium deficient bone as demonstrated by the osteoid borders in bone stained with eosin or carmine after Müller fluid decalcification. In such instances, there is a definite and prolonged time interval between the appearance of the calcium-poor zone and the removal of the calcium-poor organic matrix. In the more acute inflammatory conditions with local decalcification, the progress of the decalcification and the aggressiveness of the resorptive reaction may be so closely interrelated in time that no sooner is the bone decalcified than the decalcified matrix is removed. Under such conditions, clearcut histologic evidences of preliminary decalcification may be lacking. Even in these conditions, however, ground disks of undecalcified bone show that there is a change in the calcium salts in the vicinity of resorption, and that preliminary decalcification takes place in inflammatory diseases.

Volkmann's canals are produced in the same way. Between existing vessel canals local areas of decalcification appear which become vascularized. The appearance of threadlike cracks in the ground substance is associated with a loss of calcium along the path of the crack. The crack rapidly enlarges and grows in length, and gradually increases in width, beginning at the base which is at the haversian canal. An elongated, triangular passage is thus produced. The borders of the canal at this stage are irregular and toothed, and the canal is vascularized, but the vessel is preceded, according to Pommer,[11] by some connective tissue which seems to play a part in the opening of the crack. A Volkmann canal may become as wide as a normal haversian canal. Volkmann believed that the new canals resulted from the disintegration of bone

11. Pommer, G.: Untersuchungen über Osteomalacie und Rachitis, Leipzig, F. C. W. Vogel, 1885; Ueber den Begriff und die Bedeutung der durchborenden Knochenkanale, Ztschr. f. mikr. anat. Forsch. **9**:540, 1927.

ground substance and that lacunae and canaliculi of the bone cells rarely played a part in their production. Occasionally lacunae of the bone cells might be seen opening on a canal, but this happened only when a lacuna lay in its path. Volkmann recognized that the canals were vascularized by vessels coming from the existing haversian vessels.

The Relation of Bone Cells to Vascular Resorption.—The possibility that the bone itself is not entirely passive in resorption deserves more attention. Virchow long ago called attention to the changes in the bone cells and lacunae in resorption and believed that Howship's lacunae were produced as a result of local disintegration of the bone. Others have even derived the Volkmann canals from lacunae and canaliculi of the bone cells.[12] In inflammatory resorption, I, like many others, have frequently noted enlargement of bone cell lacunae, degeneration of the bone cells and confluence of bone cell lacunae. Although these changes occur, I do not believe they result in the formation of Volkmann's canals. They have no direct relation to vascular resorption.

OSTEOCLASTIC RESORPTION

Probably much more has been written about the resorption of bone by osteoclasts than about any of the other phases of bone resorption. Though there are those who do not ascribe functional significance to the osteoclasts, the majority opinion accepts the resorptive ability of these cells as proved. Even those who accept the resorptive powers of the osteoclasts, however, differ as to the extent and importance of this activity. Some merely acknowledge that the osteoclast can resorb bone, while at the other extreme, many declare that all resorption of bone is accomplished by osteoclasts. I am convinced that the osteoclasts are capable of resorbing bone, but I do not expect to find resorption by osteoclasts in all bone no matter what the basis for the resorption. I have seen extensive resorption of bone in the absence of osteoclasts. Such observations do not mean that osteoclasts have no bone-resorbing powers, but merely that in certain types of resorption of bone, osteoclasts play a negligible rôle. Osteoclasts may be absent or they may apparently dominate the resorptive picture. Their presence or absence depends on the cause and the course of the resorption, and they are merely an expression of the way in which the tissues are reacting to a stimulus. Osteoclastic resorption, when present, is always associated with other resorbing processes and it may come into prominence when vascular resorption is not aggressive. In conjunction with resorption of bone by osteoclasts, with the resultant formation of Howship's lacunae, so many

12. Rindfleisch, G. E.: Pathologische Gewebelehre, ed. 5, Leipzig, Wilhelm Engelmann, 1878. Thierfelder, F. A.: Atlas d. pathol. Histologie, Leipzig, Fues, 1876.

associated phenomena must be discussed, that the large amount of space devoted to osteoclastic resorption often gives an erroneous impression concerning its importance in pathologic resorption.

The process of resorption of bone by osteoclasts, resulting in the formation of Howship's lacunae, is known as lacunar erosion. Howship's lacunae appear on the periosteal or endosteal surfaces of the bone and less frequently on the walls of the vessel canals. They vary in form, but generally tend to be hemispherical depressions measuring from 30 to more than 100 microns in their greatest diameter. In or near these depressions, osteoclasts are frequently seen. These cells were first distinguished from the megakaryocytes of the bone-marrow by Robin.[13] Koelliker was the first to discuss the cause and effect relationship between osteoclasts and Howship's lacunae. Koelliker described them in the normal, physiologic resorption of growing bone, while Wegner [14] soon after discussed the presence of osteoclasts in the Howship's lacunae of pathologic bone. In certain parts of the normal growing skeleton where there is marked resorption, particularly in the jaw, osteoclasts and Howship's lacunae are present in large numbers, which is also true for certain pathologic conditions in which the resorptive process is slow and progressive.

The way in which the Howship's lacunae are formed has raised long and interesting discussions. Whether they are formed by the osteolytic activity of the osteoclast or whether these cells simply phagocytose the bone which has undergone a primary change will be discussed later. However, it is important to recognize that changes in the bone brought about by chemical and physical influences may lead to its softening, so that the bone may become more subject to cellular encroachment, or else, such changed bone may actually separate off, resulting in gouged out surfaces.

A discussion of the numerous aspects of osteoclastic resorption is necessary to show the development of the knowledge concerning these cells. When they are present in resorption they produce such a striking impression that attention is immediately directed toward them. So many conflicting reports concerning their origin, formation and function are current that a review is indicated with the perspective that osteoclasts are only a part of the process of resorption.

Origin.—Different opinions have been expressed as to the cells from which the osteoclasts originate, the conclusions having been drawn from a variety of material. Their origin has been traced from the

13. Robin, C. P.: Sur l'existence de deux epèces nouvelles d'éléments anatomiques qui se trouvent dans le canal médullaire des os, Compt. rend. Soc. de biol. **1**:149, 1849.

14. Wegner, G.: Myeloplaxen und Knochenresorption, Virchows Arch. f. path. Anat. **56**:524, 1872.

mature or embryonal connective tissue of the marrow from osteoblasts, bone cells and from the vascular or lymphatic endothelial cells. In view of the increased knowledge concerning the circulating mononuclear leukocytes and the wandering large mononuclear phagocytes of the tissues, their relation to osteoclast formation must be considered. The difficulty in tracing the origin of the osteoclasts in mammals is the fact that their formation is rapid, so that in fixed preparations it is difficult to find transition stages.

Origin from Embryonal Connective Tissue: Koelliker, Morison,[15] Jackson,[16] Dantschakoff[17] and Maximow[18] traced the origin of the osteoclasts in fetal bone to the enlarged reticulum or embryonal connective tissue cells of primary bone-marrow. Jackson described their origin from the reticulum cells of the primary marrow through mitotic division of the nuclei without protoplasmic division. Dantschakoff and Maximow also traced the origin from these cells, but they believed that osteoclasts arise as a result of the confluence of these cells without nuclear division. According to Maximow, the giant cells at first remain in contact with the adjacent embryonal connective tissue by fine anastomotic processes, but these soon disappear. The number of nuclei in these first osteoclasts is usually between three and ten, and the osteoclasts have irregular shapes. Morison expressed the belief that they may arise from the embryonic connective tissue by either multiplication or confluence. Jordan[19] recently confirmed Maximow's observations, except that occasionally he observed mitotic division of the nucleus in the early stages. Arey[20] also held that in the earliest stages of bone development, and to a lesser extent in the later stages, osteoclasts apparently arise from the confluence of primitive connective tissue cells of the marrow. It seems then definitely proved that in fetal bone the osteoclasts arise from embryonal connective tissue, probably solely by confluence of these cells.

My studies of fetal bone are confirmatory of such an origin. In a number of young fetuses, I observed osteoclast formation from the

15. Morison, A.: Bone Absorption by Means of Giant Cells, Edinburgh M. J. **19**:305, 1873.

16. Jackson, C. M.: Histologie und Histogenese des Knochenmarkes, Arch. f. Anat. u. Physiol., 1904, p. 33.

17. Dantschakoff, V.: Entwicklung des Blutes und Bindegewebes bei den Vögeln, Anat. Hefte **37**:471, 1908.

18. Maximow, A.: Experimentelle Untersuchungen ueber die entzuendliche Neubildung von Bindegewebe, Beitr. z. path. Anat. **32**:573, 1902; Untersuchungen ueber Blut und Bindegewebe, Arch. f. mikr. Anat. **76**:1, 1910-1911.

19. Jordan, H. E.: Further Evidence Concerning the Function of Osteoclasts, Anat. Rec. **20**:281, 1921.

20. Arey, L. B.: The Origin, Growth and Fate of Osteoclasts and Their Relation to Bone Resorption, Am. J. Anat. **26**:316, 1920.

embryonal connective tissue surrounding vascular sprouts which were invading the capsules of degenerating cartilage cells. Osteoclasts that appeared in the primary marrow spaces in connection with the trabeculae of primary bone also could be traced to the mesenchymal connective tissue. Osteoblasts are developed from this same mesenchymal connective tissue (fig. 12).

Origin from Mature Connective Tissue: Von Rustizky [21] described the origin of the osteoclasts from mature connective tissue. By that he probably meant the fibroblasts. His conclusions were drawn from experiments on rabbits and from a large amount of pathologic material. He described two types of osteoclasts, fixed and wandering. An origin from mature connective tissue cells (fibroblasts) seems to be contradicted

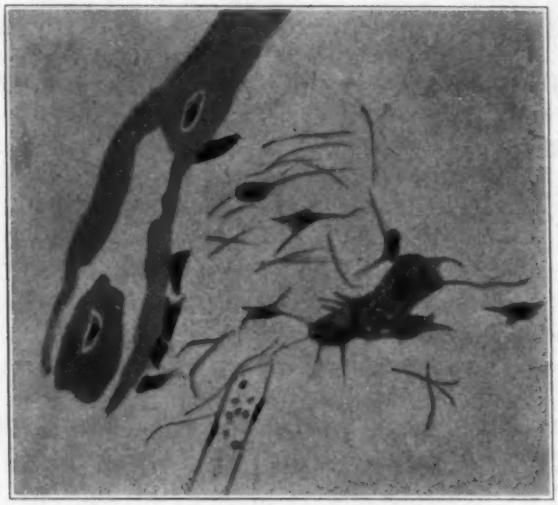

Fig. 12.—Camera lucida drawing of a primary trabecula lined by some osteoblasts. To the right a young osteoclast is seen forming by fusion of embryonal connective tissue. Some of the cells making up the osteoclast are still attached to the surrounding mesenchymal connective tissue by processes.

by the latest concepts of the connective tissues, which consider the fibroblasts as highly differentiated cells incapable of undergoing transformation into foreign body or inflammatory cells. Rustizky's views were in harmony with the ideas then prevalent concerning the origin of the giant cells in general. The theory that giant cells arose from fixed connective tissue cells originated with Virchow. This conception still has some adherents. Lubarsch,[22] as recently as 1923, mentioned that

21. Von Rustizky, J.: Untersuchungen ueber Knochenresorption und Riesenzellen, Virchows Arch. f. path. Anat. **59**:202, 1874.

22. Lubarsch, O.: Entzuendung, in Aschoff, Ludwig: Pathologische Anatomie, Jena, Gustav Fischer, 1923, vol. 1, p. 556.

most of the giant cells in inflammatory granulation tissue were derived from fixed connective tissue cells.

Origin from Osteoblasts: Assuming that osteoclasts are derived mainly or entirely from mesenchymal cells during the embryonal life, it is important to discuss their mode of origin in later life in normal and in pathologic bone.

Many of those who concede the origin of the earliest osteoclasts from embryonal connective tissue, nevertheless believe that in older bone or in diseased bone the osteoclasts are formed from osteoblasts. Even Koelliker, who is quoted as having formulated the osteoblastic theory of osteoclast formation, admits that during the erosion of the cartilaginous skeleton, he saw pictures that indicated the origin of some of the osteoclasts from mesenchymal connective tissue. Others have derived all osteoclasts from osteoblasts. The condition of the osteoblasts at the time of osteoclast formation has been variously stated, and there has also been a difference of opinion as to whether osteoclasts are formed from osteoblasts by a process of confluence or by mitosis.

Koelliker maintained that osteoclasts arise almost exclusively from osteoblasts and attain their multinuclearity by repeated nuclear divisions. Pommer [23] also believed that osteoblasts were capable of producing osteoclasts, as Koelliker described, but he did not believe that they arose exclusively from osteoblasts. Howell [24] believed that giant cells in general were formed by fusion of smaller cells in consequence of too rapid growth, and that osteoclasts in particular were probably formed by fusion of closely packed osteoblasts which were forced to coalesce. Arey expressed the belief that while in the early stages of bone development and to a certain extent in later stages, osteoclasts apparently arise from the confluence of mesenchymal and connective tissue cells of the marrow, the chief source of osteoclasts is from old osteoblasts and bone cells. He stated that the depleted basophilic osteoblasts coalesce to form multinucleate masses. These syncytial elements become typical osteoclasts when their cytoplasm assumes oxyphilic properties. He found intermediate tinctorial and transitional stages. On the other hand, Jordan, while tracing most of the osteoclasts from the marrow reticulum, found that during later stages osteoclasts also arise from young, slightly differentiated osteoblasts, by fusion.

While these authors admit an origin of osteoclasts either entirely or partly from osteoblasts, there is no unanimity of opinion as to whether the osteoblasts are depleted or physiologically active, or whether

23. Pommer, G.: Ueber die Osteoblastentheorie, Virchows Arch. f. path. Anat. **92**:296, 1883.

24. Howell, W. H.: Observations Upon the Occurrence, Structure and Function of the Giant Cells of the Marrow, J. Morphol. **4**:117, 1890-1891.

the process is one of nuclear division without division of the protoplasm or one of cell confluence.

Studying many sections from a variety of material, I have not found convincing evidence of the origin of osteoclasts from osteoblasts. While I have frequently seen large clumps of osteoblasts on trabeculae, generally these clumps were made up of cells which always maintained their individuality. Where there were evidences of nuclear and cytoplasmic degeneration in these cells, no definite evidence of fusion was observed. In specimens of adult bone decalcified in Müller's solution and stained with eosin and methylene blue, the cytoplasm of the individual osteoblasts and clumps of osteoblasts was always basophilic, while the osteoclasts, no matter how small and no matter how few the nuclei, always had acidophilic cytoplasm. My studies lead me to reject the conception that osteoclasts are formed from osteoblasts, and this holds for both embryonal and adult bone.

Origin from Bone Cells: In regard to the origin of osteoclasts from bone cells, Bredichin [25] stated that the giant cells are a stage in the process of the transformation of bone into marrow and granulation tissue. A similar view was held by Kassowitz,[26] who, however, believed that at first there was an increased vascularization of the bone and decalcification, following which the bone cells proliferated to form giant cells. Loewe [27] believed that the osteoclasts arose from bone that was decalcified after its separation from the main bone mass. Finally, these osteoclasts break up into as many individual cells as there are nuclei, and disperse themselves in the bone-marrow. Lang [28] also believed that the giant cells arose mainly from bone cells. While bone cells may be taken up by osteoclasts, several authors having actually observed their phagocytosis by giant cells, an origin of osteoclasts from bone cells seems untenable.

Origin from Vascular Channels: Wegner observed a close association between osteoclasts and blood vessels in pathologic bone. He believed that in bone resorption osteoclasts arise by proliferation of the vessel wall, and that these osteoclasts erode the bone as they are proliferating. Wegner is not clear as the details of such an origin. He does not state whether these cells arise from the lining endothelial cells or from the perivascular endothelium, or from the muscular and connective

25. Bredichin, J.: Ueber die Bedeutung der Riesenzellen im Knochen, Centralbl. f. d. med. Wissensch. **5**:563, 1867.

26. Kassowitz, M.: Die normale Ossification und die Erkrankungen des Knochensystems, Med. Jahrb., 1879, pp. 145 and 293.

27. Loewe, L.: Ueber die Umwandlungen der Osteoklasten im Knochenmark nebst Bemerkungen ueber Knochenwachstum, Arch. f. mikr. Anat. **16**:618, 1879.

28. Lang, E.: Untersuchungen ueber die ersten Stadien der Knochenentzuendung, Med. Jahrb., 1871, p. 34.

tissue elements of the wall. Others, among them Maas,[29] expressed an intimate relation between the osteoclasts and the vessel walls, though they did not state that the cells are actually derived from the vessel walls.

The Foreign Body Giant Cell Conception of Osteoclasts.—Throughout the literature on osteoclasts the idea frequently recurs that osteoclasts are related to the giant cells found in a wide variety of conditions. Mallory [30] made a definite statement to that effect. Haythorn,[31] in a recent review of the subject, accepted this point of view and he said that most modern writers group the Langhans' cell of tuberculosis, the common foreign body giant cell and the osteoclasts as one cell type which forms in response to a stimulus and which varies morphologically only with local environmental influences. The view that the osteoclasts are functionally and genetically related to foreign body giant cells is an important conception and one that is helpful in explaining the origin of osteoclasts in pathologic resorption during adult life. It seems logical that injured, decalcified or dead bone that shows no regenerating tendency becomes essentially a foreign body, and the cells in contact with it try to remove it.

To enter into a detailed discussion of the origin of the foreign body giant cell as a basis for the understanding of the origin of the osteoclast of later life would take me too far afield. Moreover, this has recently been well down by Haythorn. The opinion is that foreign body giant cells are derived from the mononuclear leukocytes of the circulation and wandering cells of the tissues. Whether mononuclear leukocytes arise from vascular or lymphatic endothelium (Mallory), whether they are transformed cells of the marrow (Sabin) or circulating blood cells (Maximow), or whether they come from the reticuloendothelial system (Aschoff) and what their connection is with the wandering cells of the tissues are problems that have not been settled. Whatever the exact origin of the wandering large mononuclear phagocyte of the tissues may be, and whether they represent a single specific cell or a group of allied cells, these cells and the mononuclear leukocyte are concerned in the formation of the foreign body giant cell and consequently the osteoclast of later life.

The relation of the osteoclast to the foreign body giant cell has been stressed, and I believe must be accepted. From a study of the literature and from my own observations, it appears that the osteoclast in embryonic life is derived from the mesenchyme, and that in later life, under both normal and pathologic conditions, the osteoclast is

29. Maas, H.: Ueber das Wachstum und die Regeneration der Rochrenknochen, Arch. f. klin. Chir. **20**:718, 1877.

30. Mallory, F. B.: Giant Cell Sarcoma, J. M. Research **19**:463, 1911.

31. Haythorn, S. R.: Multinucleated Giant Cells, Arch. Path. **7**:651 (April) 1929.

a reactive cell arising by fusion of the resting wandering cells of the tissues supplemented by the mononuclear cells of the circulation. It seems to me that the theory of an origin by osteoblastic fusion or proliferation must be abandoned. Osteoblasts and bone cells may be present in osteoclasts; if so, they are present by virtue of phagocytosis.

Morphology.—The appearance of the individual osteoclast varies considerably. The osteoclast may be either small or large and may contain a few or as many as 100 nuclei. Large, fully developed osteoclasts are elongated, flat, multinucleated cells of irregular shape, without a definite limiting membrane. Koelliker recorded their maximum size in the new-born infant as from 43 to 91 microns in length, from 30 to 40 microns in width, from 16 to 17 microns in thickness, and with as many as fifty or sixty nuclei. Arey found the measurements in the embryonal pig to run as high as from 65 to 105 microns, with a nuclear count of about 125. Smaller mature osteoclasts may contain as few as five nuclei or less and be no more than from 6 to 10 microns in the largest diameter. The first osteoclasts formed during embryonal bone formation usually have between three and five nuclei. Osteoclasts often fuse to form large syncytial masses.

Some osteoclasts have been described with simple, branched or pseudopod-like processes, and Dantschakoff, Maximow and Arey believed that osteoclasts were capable of ameboid motility, but Koelliker failed to confirm ameboid motility in living osteoclasts, examined on a warm stage. That they are capable of moving about is evident from the facts that they frequently are outside of the Howship's lacunae, and that they may be seen entering capillary vessels (fig. 13).

The cytoplasm of osteoclasts encountered in adult or in pathologic bone is strongly acidophilic. While some have observed osteoclastic cytoplasm in all tinctorial stages from basophilic to acidophilic, I have not observed a cell that I could with certainty call an osteoclast, except in embryonic life, that contained any but acidophilic cytoplasm. The cytoplasm is granular, sometimes coarsely so. When stained according to Foot's [32] modification of the Bielschowsky-Maresch silver impregnation method, the cytoplasm of osteoclasts contains large, coarse, black granules (fig. 14). A variable number of vacuoles is present, but whether these are fat has not been definitely proved.

The nuclei are round or obliquely round and tend to be pyknotic, especially in the older, apparently degenerating forms. One or two nucleoli may be seen in varying positions. Some nuclei appear shrunken or folded, but convincing amitotic stages have not been observed by Maximow, Arey and others. Koelliker reported finding

32. Foot, N. C.: Chemical Contrast Between Collagenous and Reticular Connective Tissue, Am. J. Path. **4**:525, 1928.

some division figures, but most of those who focused their attention on this point were unable to confirm the observation. Maximow, though not denying the possibility, stated that he never observed mitotic or amitotic division figures in the material he examined. In pathologic material, I never observed mitotic division figures.

Certain osteoclasts exhibit a brush border along the edge in apposition with the bone. Koelliker and Wegner were among the first to make this observation. Arey observed this particularly in the osteoclasts of cattle. Maximow even observed such borders on some of the foreign body giant cells. In dogs suffering from experimental osteoporosis, I have occasionally observed such borders. This border

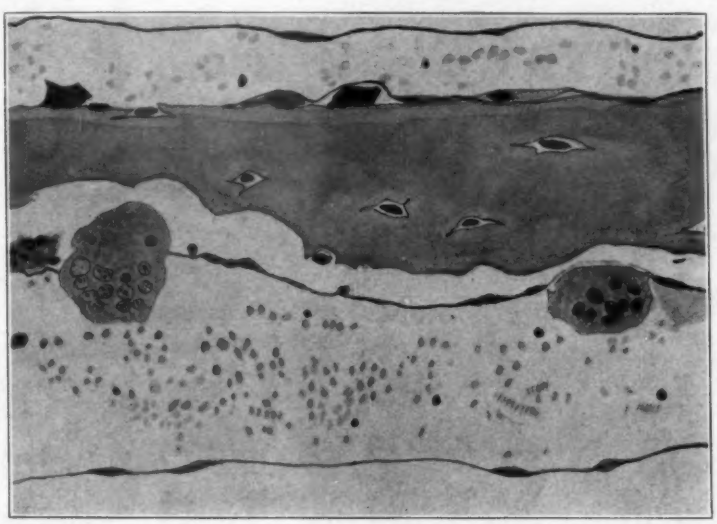

Fig. 13.—Camera lucida drawing, showing a spongy trabecula from the marrow cavity of a rib of a dog suffering from osteoporosis. The lower surface of the trabecula shows resorption, osteoblasts having disappeared. Some Howship's lacunae and an opened bone cell lacuna are seen. One osteoclast is seen in, and another is seen entering a dilated capillary adjacent to the trabecula. Magnification about 600.

stains more intensely than the rest of the cell and may be finely striate or composed of coarse elements. Some osteoclasts have a fringed or toothed appearance, while others are observed with fibers and fibrils, the free edges of which extend from the cell and are in contact with the surrounding tissues.

Function.—In spite of some negative statements in the literature, it may be accepted that osteoclasts are capable of removing bone. I mean to include here their ability to erode bone directly, as they sometimes appear to be doing when they are in Howship's lacunae and also

the ability to phagocytose dead bone. But how important this function is, in resorption of bone, is open for discussion. Koelliker was the first and most persistent exponent of their bone-destroying function. He believed that their presence in the Howship's lacunae of resorption surfaces demonstrated this function beyond controversy. Among the many who have subscribed to this view were Wegner, Morison, Jackson, Maximow and Jordan. Mallory even suggested that the erosion of bone may be accomplished mechanically by the brush border of the osteoclast. Schaffer [33] likewise held that osteoclasts have a bone-destroying action. Jordan described the presence of small spicules of bone within some osteoclasts, which he believed were phagocytosed. Using Foot's modification of the Bielschowsky-Maresch silver impregnation technic, I have also observed osteoclasts containing fragments of bone. These fragments stained like the collagen fibrils of the bone (fig. 15).

Fig. 14.—High power camera lucida drawing of part of a trabecula from the medullary cavity of an osteoporotic rib of a dog. A deep Howship lacuna is seen containing an osteoclast which fits snugly into the lacuna. The osteoclast shows numerous coarse dark granules. Paraffin section, Bielschowsky-Maresch silver stain.

In spite of much evidence in favor of either a phagocytic or an osteolytic function of the osteoclasts, some definite denials of such function have appeared. Strelzoff [34] did not believe that osteoclasts could resorb bone. Ziegler [35] doubted the resorptive function of osteoclasts, because he believed that the osteoclasts seen in numerous bone conditions were genetically unrelated. Howell opposed the probability of

33. Schaffer, J.: Die Verknoecherung des Unterkiefes und die Metaplasiefrage, Arch. f. mikr. Anat. **32**:266, 1888.

34. Strelzoff, Z. J.: Ueber die Histogenese der Knochen, Unters. aus d. path. Instit. zu Zurich, Herausg. v. C. Eberth, Leipzig, 1873.

35. Ziegler, E.: Ueber Proliferation, Metaplasie und Resorption des Knochengewebes, Virchows Arch. f. path. Anat. **73**:355, 1878.

osteolytic function, believing that the formation of osteoclasts in embryonic life or in pathologic conditions was accidental, owing to rapid growth and fusion of the cells. Lewis [36] thought that there was no satisfactory evidence that the osteoclasts were active causes of bone destruction, and believed that they were degenerating cells. Arey recently stated that only indirect and insufficient evidence points to osteoclasts as active, specific agents of bone resorption. To him they are merely degenerating, fused osteoblasts. Arey would attribute to them the capacity of phagocytosis but not osteolysis. Furthermore, he stated that the mere presence of cytoplasmic inclusions within an osteoclast by no means indicates that the latter was responsible for the dissolution of the material ingested.

Arey takes issue with those who use "osteolytic" as a term interchangeable with "phagocytic." In the true sense, osteolysis by osteo-

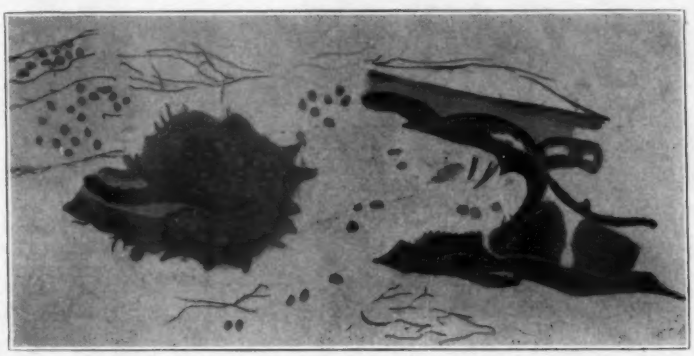

Fig. 15.—High power camera lucida drawing of a trabecula from the marrow cavity of a dog suffering from osteoporosis. On the right there is a Howship's lacuna with a fringed border. On the left is an osteoclast containing a large piece of phagocytosed bone. Paraffin section, Bielschowsky-Maresch silver impregnation.

clasts implies the direct dissolution of unchanged bone by these cells. Phagocytosis of the bone implies the removal of changed bone. Whether osteoclasts are capable of osteolysis or phagocytosis of bone depends on whether the osteoclasts dissolve the inorganic salts before they remove the organic matrix. There is no direct way of proving this, and it seems that most authors have not distinguished between osteolysis and phagocytosis in regard to bone. If such a distinction is to be made, then the function of the osteoclast is certainly that of a phagocyte. Whether it can also dissolve the bone directly cannot be answered at present. On the basis of available knowledge it would be better to think of the

36. Lewis, F. T.: A Text-Book of Histology, Philadelphia, P. Blakiston's Son & Company, 1913.

osteoclasts as bone resorbers rather than as bone dissolvers. Large osteoclasts may be observed within the blood vessels of the marrow. That such gain admittance and do not arise in situ from the endothelium is supported by their degenerated appearance. I have observed such osteoclasts in the marrow vessels, and believe that much of the bone which they phagocytose is removed in this way.

The observations refuting the resorptive ability of osteoclasts are that Howship's lacunae may be seen without osteoclasts, and often in inflammatory diseases there may be extensive resorption of bone also without osteoclasts, especially in acute fulminating osteomyelitis. These observations do not prove that osteoclasts are not resorbing agents, but serve only to emphasize what I have said before, that there are other types of bone resorption besides the osteoclastic type. From my experience it appears that in the more acute inflammatory diseases of bone, erosion by osteoclasts is unimportant. On the other hand, in the less acute inflammatory processes, osteoclasts are numerous and seem to be playing a signiflcant part in the resorption.

In summary, I believe that osteoclasts are capable of resorbing bone but they are of secondary importance in resorption of bone. Whenever osteoclasts are resorbing bone, there is also vascular resorption, but vascular resorption may under certain circumstances be so extensive that it may completely overshadow osteoclastic resorption. Osteoclastic resorption is more likely to be seen in the slower resorptive processes and since osteoclasts in later life are formed like other foreign body giant cells, they occur more frequently in chronic inflammations. I believe that they are active aggressive cells capable of removing the bone. The bone at the time of its removal by osteoclasts is undoubtedly decalcified, but how much, if any, of the decalcification is produced by the osteoclasts, cannot be answered.

Fate.—Most opinions pertaining to the fate of osteoclasts either uphold the theory of their transformation into other cellular elements or suggest their total destruction, or admit both possibilities. Ribbert believed that the osteoclasts disintegrated and disappeared like the giant cells of giant cell tumors. Bredichin thought them to be transitional stages in the transformation of bone tissue into marrow and granulation tissue. Wegner believed that they became transformed into spindle connective tissue cells, but, observing that some had passages, was led to speculate as to whether new blood vessels might arise from osteoclasts. Koelliker suggested that after their resorptive activity has ceased the osteoclasts may divide into osteoblasts and resume bone formation, but he found no definite proof of this. Morison denied it. Koelliker also considered their degeneration or transformation into connective tissue or marrow cells. Jackson and Maximow have upheld the fragmentation of osteoclasts in the embryo into detached cells which

became indistinguishable from the reticulum of the marrow. But in adults, according to Maximow, the osteoclasts never revert in this way, always undergoing degeneration and disappearing. This also holds true to some degree in the embryo, and Jordan believed that osteoclasts of the embryo disappear by degeneration. Most likely, osteoclasts finally either degenerate locally or enter blood vessels and are removed in this way.

Howship's Lacunae: Their Relation to the Osteoclasts.—Howship's lacunae always appear on the surfaces of bone, arising subperiosteally or under the endosteum or on the surface of the vessel canals, but they do not appear within the substance of the bony trabeculae or lamellae. According to Koelliker, the lacunae are smooth and have sharp borders and are bordered by normal bone. The lacunae are sometimes rounded and sometimes irregular. Pommer described fringed or brushlike borders on some lacunae produced by fibrils or fibril bundles which remained preserved on dissolution of the ground substance. He believed that he could trace them to the fibrils of the surrounding lamellae. In sections stained by Foot's modification of the Bielschowsky-Maresch technic I have frequently observed such lacunae (fig. 15). Pommer observed osteoclasts with finely fringed borders, matted with the brush borders of lacunae. The osteoclasts may conform to the shape of the lacunae, but their form is often more varied than that of the lacunae. The frequency with which osteoclasts are related to lacunar erosion is difficult to judge, because it is known that with the cessation of the resorptive activity, the osteoclasts disappear and connective tissue, marrow or granulation tissue replaces them. Then new bone may be deposited on the walls of the lacunae by osteoblasts which line them. When the lacunae no longer contain osteoclasts, Pommer believes that resorption has ceased. It is known that lacunae occur in resorbing bone without containing osteoclasts. The cause and effect relationship between Howship's lacunae and osteoclasts is generally admitted (fig. 16), but the manner in which the lacunae are formed and the part that osteoclasts play in their formation seem never to have been definitely settled.

In regard to the part that the ground substance plays in the formation of Howship's lacunae, Pommer [23] has often stated that it is entirely passive and that lacunar resorption is in no way dependent on preparatory decalcification of the ground substance. According to him, lacunar erosion takes place the same way in calcium-free and in normal bone. Von Recklinghausen [37] has shown conclusively that in osteomalacia the resorption of bone is preceded by the removal of calcium. The extent of the preliminary decalcification of the ground substance

37. Von Recklinghausen, F.: Untersuchungen ueber Rachitis und Osteomalacie, Jena, Gustav Fischer, 1910.

in resorption of bone due to inflammation is not conclusively settled, though Volkmann believes that there is evidence of such a process, and Ribbert thinks that it occurs in all normal pathologic resorption.

I believe that in the formation of Howship's lacunae, preliminary decalcification plays an important rôle. A Howship lacuna is probably formed as follows: Resorption is initiated when bone formation ceases. Then a decalcifying influence is exerted on the bone which varies with the etiologic factor of the resorption. Just what decalcifies the bone is not known. The various possibilities were discussed under vascular erosion. It may be changed p_H or local lactic acid production or changed local carbon dioxide tension. Whatever this factor is, it exerts an

Fig. 16.—Section through bony callus of a healing fractured rib in a dog suffering from osteoporosis. Numerous osteoclasts are seen occupying Howship's lacunae in the process of reconstruction of the callus. Paraffin section, Müller decalcification, eosin and methylene blue stain; × 75.

effect on the surfaces of the spongy trabeculae, just as it does on the walls of the haversian canals or anywhere else. Osteoclasts arising locally as reactive, resorptive cells then remove the decalcified bone. The stimulus to osteoclast formation varies with the resorptive processes. I doubt whether the osteoclasts themselves exert a dissolving influence on the bone before they remove the ground substance, but unequivocal evidence in either direction is unavailable.

The Relation of Howship's Lacunae to Bone Cells.—In regard to the behavior of the bone cells and their processes in lacunar resorption, many believe that they are entirely passive and that the cells in closed

lacunae never show changes. Opened bone cell lacunae either are empty or contain cells not much altered. The bone cells may degenerate and are then phagocytosed by the osteoclasts. On the other hand, some believe that the bone cells may produce lacunar resorption and Howship's lacunae. Virchow was the originator of this conception and described the formation of Howship's lacunae as due to fatty metamorphosis of the bone cells, followed by their enlargement and nuclear division. Concomitantly with the nuclear division, changes in the ground substance occur and spherical or elongated masses of the ground substance are split off and continue to disintegrate into granules, leaving cavities, the Howship's lacunae. Virchow had numerous supporters of his view. It is, of course, true that in inflammatory diseases of bone, regressive changes, such as fatty metamorphosis and degeneration of the bone cells, occur, but not constantly. While Virchow's theory has had supporters, a greater number of workers have felt that the progressive changes in the bone cells were related to lacunar resorption because they proliferated to form giant cells which produce the Howship's lacunae.

That the bone cells play an active part in resorption was denied by Koelliker, Billroth and Volkmann, who have often demonstrated experimentally that bone cells in the vicinity of Howship's lacunae do not have enlarged cavities. However, the observation of Virchow that in resorptive processes the bone cell lacunae enlarge can easily be confirmed on examining bone from a variety of resorptive processes. The observation is more common when inflamed bone is examined. As I have stated, in some instances the appearance of lamellar bone may be so changed by the enlargement of Howship's lacunae that in a decalcified section stained with hematoxylin and eosin such bone may look like fiber bone. I have seen large spaces formed within the substance of spongy trabeculae by the coalescence of enlarged lacunae. Such observations are probably dependent on circulatory disturbances in the bone, possibly on thrombosis of vessels leading to the bone. I do not believe that degeneration of the bone cells and enlargement of the bone cell lacunae are important in the actual resorption of bone, but such bone is more subject to resorption.

LOCALIZED BULBAR CISTERNA (PONTILE) MENINGITIS, FACIAL PAIN AND SIXTH NERVE PARALYSIS AND THEIR RELATION TO CARIES OF THE PETROUS APEX*

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I. FACIAL PAIN

Gradenigo syndrome of sixth nerve paralysis, associated with fifth nerve pain and a discharging ear, has been the subject of numerous communications, the general trend of which would give the impression that the abductor paralysis results from pressure on the nerve either (*a*) by the petrosphenoidal (Gruber's) ligament as the nerve passes over the petrous apex secondary to swelling of the bone of the petrous apex or (*b*) it is the manifestation of a localized meningitis in the neighborhood of the nerve. In a few cases sixth nerve paralysis has been regarded as resulting from (*c*) neuritis of toxic origin.

The prognosis is generally regarded as favorable. All authors advocate the prompt opening of the mastoid when the neurologic symptoms appear early in the course of an otitis; while in the cases in which the syndrome develops subsequent to the operation, delay in further operating is advocated, as both the paralysis and the pain usually disappear spontaneously.

FATAL CASES OF GRADENIGO SYNDROME

Gradenigo pointed out that in many cases there was an associated extradural abscess; and Sears,[1] in a compilation of the literature, found that in nearly 20 per cent of all the reported cases the patients died from an intracranial complication.

In spite of this high mortality, little attention has been paid to the possibility of the early recognition of the type of case in which meningitis develops although a mastoid operation may have been performed.

OBJECTS AND METHODS OF INVESTIGATION

The first object of this communication and the dissections on which it is based was (1) to determine the various anatomic factors that may cause facial pain and sixth nerve paralysis in suppuration of the

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1. Sears, W. H.: Otogenic Paralysis of the Abducens, with Especial Mention of Isolated Palsy Associated with Irritation of the Gasserian Ganglion, Tr. Am. Laryng. & Otol. Soc., 1925, p. 89.

petrous and meninges. For with the exception of Baldenweck,[2] no attempt has been made to solve the problems presented by the Gradenigo syndrome—(*a*) why it occurs in one case of suppuration in the mastoid and not in another, as well as (*b*) what anatomic peculiarity excites a contralateral abductor paralysis—by the obviously direct method of studying the anatomic relationships of the petrous apex and its neighborhood as found in a succession of cadavers. (*2*) The second object is to apply the knowledge obtained from dissections to the clinical differentiation between the cases in which recovery occurs and those in which intracranial complications uniformly develop, in order that the latter group may be promptly recognized and surgically attacked at an early date. It is only during the primary stage of the meningeal process that surgical intervention promises some measure of success in the admittedly large percentage (20 per cent) of cases which otherwise end fatally.

Experimental Methods Employed in Anatomic Dissections.—The surgical anatomy described is based on the dissection of eight embalmed cadavers (placed at my disposal by Professors F. Lemaitre and G. Rouhier of Paris). In seven cadavers, the (*a*) arachnoid prolongation surrounding the internal auditory meatus, or the (*b*) meshes of the arachnoid in the region of the posterior fossa just superior to the jugular bulb were opened, into which a solution of dye was introduced and from them allowed to diffuse by gravity through the spaces of the arachnoid.

Anatomic Basis of Facial Pain and Sixth Nerve Paralysis.—During the dissection on the cadavers an effort was made to ascertain an anatomic basis for sixth nerve palsy and fifth nerve pain in the various types of osteitis, phlebitis and meningitis.

FACIAL PAIN IN SUPPURATIVE OTITIS DIAGNOSTIC OF MIDDLE FOSSA INVOLVEMENT

Facial pain in suppurative disease is diagnostic of middle fossa involvement because the gasserian ganglion and the other nervous elements that may contribute to the production of facial pain lie anterior to the tentorium. Posterior fossa inflammation does not cause facial pain; for although the sensory root of the fifth nerve is in the posterior fossa, the pia-arachnoid prolongation surrounding it is so loose that pressure from inflammation of the bone of the posterior surface of the petrous or of the dura covering it cannot affect it. Even after the exit of the root through the ringlike opening in the tentorium, above the superior

2. Baldenweck, Louis: Étude anatomique et clinicale sur les relations de l'oreille moyenne avec la pointe du rocher, le ganglion de Gasser et la sixième paire cranière, Thèse de Paris, 1907-1908.

border of the petrous, the outer portion of the ganglion as well as its second and third branches lie free in the cerebrospinal fluid. The arachnoid prolongation extends halfway across the floor of the middle fossa, up to a line opposite the foramen spinosum. Dye introduced into the arachnoid spaces of the posterior fossa uniformly reaches this point. Suppurative leptomeningitis does not cause facial pain. It is only on its mesial side that the semilunar ganglion has dural adhesions. It is this freedom from pressure that explains the absence of facial pain in those cases of suppurative meningitis in which the bulbar cisterna is the seat of a firm exudate without involvement of the dura of the middle fossa.

Inflammation in the arachnoid irritates the tissue of the brain cortex and causes fever, headaches, restlessness, etc.; but localized pain from irritation of the sensory nerves after they emerge from the brain is induced only by direct pressure, because immediately on coming in contact with the arachnoid, the sensory nerves acquire a surrounding sheath—a combination of mesoblastic and ectoblastic tissue—the sheath of Schwann.

Facial Pain of Peripheral Not Central Origin.—When, however, that portion of the floor of the middle fossa, which is formed by the superior surface of the petrous pyramid internal to the eminentia arcuata, is the seat of inflammation, either (*a*) the ganglionic portion of the trigeminus, (*b*) a branch or branches of the fifth nerve itself or (*c*) one of the sensory elements of the facial, glossopharyngeal, vagus or cervical nerves may be irritated. In suppurative inflammation the resulting localized facial pain is largely due to the intimate relation of these sensory nerves or their communications with the bone of the cranial base posterior to the sphenopetrous suture, in which region the dura is closely adherent to the bone.

PATHOLOGIC DIFFERENCES BETWEEN CASES OF REFERRED AND DIRECT FIFTH NERVE PAIN

All cases of facial pain that disappears after the simple evacuation of the mastoid are probably caused from irritation of one of the sensory communications of the fifth and not of the trifacial nerve.

However, in cases of caries of the petrous apex, the resulting pain is probably occasioned by direct irritation of the semilunar ganglion or its first branch because of their dural adhesions; and this type of pain is not apt to be influenced by a mastoid operation.

(*a*) *Referred Facial Pain; Pain from Irritation of Sensory Nerves on the Floor of the Middle Fossa having Communication with the Fifth Nerve.*—In cases in which the irritation originates from the external two thirds of the temporal bone—the middle ear, mastoid and

labyrinthine area (that is, the area external to the outer lip of the gasserian ganglion)—the accompanying facial pain probably has nothing to do with the gasserian ganglion, although referred to one or other of its branches, because of the overmastering command that the trifacial nerve has over the dura of the middle fossa.

Irritation, then, of the sensory elements from congestion or edema of the cells in the superior surface of the petrous may occasion pain in one or other branches of the trifacial nerve, and this without involving the gasserian ganglion itself, although both the facial and the glossopharyngeal nerves have communication with the gassarian ganglion (under which they lie) and with its dural covering, from which it is difficult to separate the nerves by dissection.

Mechanism of Referred Facial Pain.—The anatomic requirements in nervous tissue necessary for the reference of pain from a visceral area to a body surface are: (1) ganglion cell fibers carrying impulses toward the central nervous system from both a visceral region and a body surface located in proximity in the same sensory ganglion, while sensory impulses from both sets of cells pass together to the brain (Head [3]); or (2) "impulses from afferent visceral fibers transferred to somatic ganglion cells in a dorsal root ganglion or its equivalent."

In man, the trifacial nerve assumes most of the sensory elements found in the facial, auditory, glossopharyngeal and vagus nerves of vertebrates possessing a lateral line nervous system; however, Hunt,[4] clinically, and Larsell and Fenton,[5] histologically, have demonstrated that the great superficial petrosal of the facial and the small superficial petrosal from the glossopharyngeal nerves contain sensory fibers, and as both nerves lie in bony canals on the superior surface of the petrous, any inflammatory swelling may cause a neuralgia from irritation.

On the superior surface of the petrous, confined in bony grooves, is the geniculate ganglion of the facial nerve from which runs the great superficial petrosal and the great deep petrosal, the latter with "myelinated fibers of the glossopharyngeal and unmyelinated postganglionic fibers from the superior cervical ganglia by way of the carotid plexus." Both unite to form the vidian which latter communicates with Meckel's (sphenopalatine) ganglion.

Irritation of the superficial petrosal of the facial nerve may cause pain referred to the second branch of the fifth nerve, because of the

3. Head, H.: The Pathology of Herpes Zoster, Brain, 1893, vols. 16 and 17.

4. Hunt, Ramsay: Sensory System of the Facial Nerve and Its Symptomatology, J. Nerv. & Ment. Dis., 1909, vol. 36.

5. Fenton, R. A.: Mechanism of Pain Transmitted in Certain Types of Otalgia, First International Oto-Rhino-Laryngological Congress, Copenhagen, 1928. Larsell and Fenton: Embryology and Neurohistology of Sphenopalatine Ganglion Connections, Tr. Am. Otol. Soc., 1928.

communication of the great superficial petrosal through Meckel's ganglion which is attached to the second branch. Larsell and Fenton have demonstrated that the sensory fibers pass through the sphenopalatine without entering the ganglion itself.

Lateral to the hiatus, in which lie the geniculate ganglion and the superficial petrosal, there is a smaller canal for the lesser superficial petrosal which passes to the otic ganglion.

Irritation of the small superficial petrosal through its connection with the otic ganglion which is attached to the third, may thus occasion a referred pain in the lower facial region.

(*b*) *Sensory Elements of the Glossopharyngeal Nerve.*—The glossopharyngeal nerve in its intradural portions is probably a special sense nerve devoted to gustatory and secretory functions (Fay [6]), but its communicating fibers which ascend through the temporal bone and reenter the cranial cavity through Jacobsen's tympanic plexus to the small superficial petrosal and by the small deep petrosal and the carotid plexus in the floor of the middle fossa probably contain sensory elements. The great deep petrosal formed by the small deep petrosal and fibers from the carotid plexus and Jacobsen's plexus probably obtain their fibers from the petrosal ganglions.

Muscular Involvement of the Fifth Nerve in Suppurative Lesions from Irritation of the Glossopharyngeal.—In suppurative disease, facial pain with trismus may follow irritation of the tympanic plexus of the glossopharyngeal (Jacobsen's) such as may be caused by a plug of cotton in the external canal of the middle ear causing a congestion of the deeper parts (Uffenorde's case [7]).

Pain of Vagus and Cervical Origin Referred to a Region Supplied by the Fifth Nerve.—Whether the vagus, which sends sensory fibers to the posterior part of the ear, and the cervicals, through communication with the carotid plexus, have sensory elements is still doubtful, but there is clinical evidence that vagal and possibly cervical plexus elements are among the causes of the continuation of the pain in some of the patients who continue to suffer after a complete resection of the sensory root of the trifacial nerve.

Rôle of Peritubal and Supralabyrinthine Cells in Referred and Direct Facial Pains.—The peritubal cells are situated just below the surface of the petrous posterior to the suture between the petrous bone and the squama and the angle formed by the squama and the greater wing of

6. Fay, Temple: Observations and Results from Intracranial Section of the Glossopharyngeus and Vagus Nerves in Man, J. Neurol. & Psychopath. **8**:110, 1927.

7. Uffenorde, W.: Disturbances of the Trigeminus Originating in the Ear, München. med. Wchnschr. **73**:2064, 1919-1920.

the sphenoid. They extend inwardly, posterior to the styloid foramen and anterior to the carotid canal.

There is thus formed a direct line of cellular tissue from the anterior part of the middle ear to the plane of the foramen spinosum,[8] and these cellular elements, especially in pneumatic mastoid, are liable to congestion. In addition, there are at least four tracts of cells along the posterior-superior surface and under the curve of the superior semicircular canal,[9] all of which tend to coalesce at the petrous apex.

Characters of Referred and Spasmodic Pains.—Although the pain of suppurative disease confined to the external one third of the temporal bone may be referred to one or other regions of the trifacial nerve, the pain is of quite a different character from the neuralgia of a true tic; the former is largely a headache associated with a peripheral or aching pain in the teeth or around the eye, while a true trifacial neuralgia is a sharp piercing spasmodic stab in the course of the nerve.

Differential Characteristics Between the Referred Pain of Suppurative Lesions of the Bone and Ganglionic Disease Probably From a Filtrable Virus.—Geniculate Ganglion Zoster.—Clinically, there is reason to believe that true zoster is a disease of the sensory elements derived from the ganglionic crest which in lower vertebrates form the spinal ganglions, the sheath cells and the sympathetic, as zoster attacks only the segmental sensory nerves.[10] The pain associated with the polyneuritis from nonsuppurative disease of the geniculate ganglion is referred externally to the ear and mastoid surface and is associated with herpes of the external auditory canal, the characteristics of the Ramsay Hunt syndrome.[4]

The pain which accompanies suppuration from geniculate ganglion involvement associated with congestion of the deep cells of the temporal bone is apt to be referred inwardly to the branches of the fifth nerve.

Conclusions Concerning the Osseous Origin of Referred Facial Pain, in Cases with Recovery After Mastoid Operation.—(*a*) The facial pain in the majority of the benign cases is undoubtedly primarily of osseous origin, because as a rule it promptly disappears when the cellular caries of the mastoid and perilabyrinthine cells is removed. (*b*) The facial neuralgia is caused by a congestion of the peritubal and superior labyrinthine cells of the anterior surface of the petrous pyramid, either of which may extend to the region of the sensory communications of the facial and glossopharyngeal nerves as they lie on the superior sur-

8. Girard, L.: Perilabyrinthine Cells, Soc. de laryngol. d'otol. et de rhinol. de Paris, Dec. 9, 1911.

9. Siebenmann, Friedrich: Die Korrosions-Anatomie des Knochernen Labyrinthes des menschlichen Ohres, Wiesbaden, J. F. Bergmann, 1890.

10. Head and Campbell: The Pathology of Herpes Zoster, Brain, 1900. vol. 23.

face of the petrous bone, communications of which pass beneath the gasserian ganglion. (*c*) Irritation in this region may originate pain which is transmitted forward to one of the trifacial peripheral elements of the first, second or third branch. (*d*) Pain of the geniculate ganglion from a filtrable virus—a polyneuritis—is transmitted externally to the drum membrane, external auditory canal or mastoid region.

From an operative standpoint, it may be stated that (1) a temporofacial pain, or a neuralgic pain in the supra-orbital region around the eye or in the face or teeth, associated with or following an otitis, if unaccompanied by signs of sepsis, cerebral irritation or labyrinthitis simply calls for the complete exenteration of the mastoid cells with as much of their perilabyrinthine cellular elements as have direct communications which can be demonstrated macroscopically. (2) This having been done, the continuation of the facial pain only becomes of serious moment if the sepsis continues.

(*c*) *Facial Pain from Direct Irritation of the First Branch.*—When, however, that portion of the floor of the middle fossa which is formed by the superior surface of the petrous internal to the eminentia arcuata is the seat of inflammation, the trifacial nerve itself may be irritated.

If the suppurative process (congestion or caries) involves the petrous apex, the resulting pain is apt to involve the first branch. Such a pain never occurs in suppuration confined to the posterior fossa.

The Significant "Pain Behind the Eye" in Suppurative Otitis.—Pain in the first branch limited to the region behind the eye is significant of irritation of the dura over the petrous apex, and in the presence of continued sepsis, signifies caries of the petrous apex.

Ophthalmic Branch a Spinal Nerve.—The ganglionic portion of the first branch of the fifth nerve is separate morphologically and developmentally from the rest of the nerve. The ophthalmic branch is in reality the highest dorsal spinal nerve as from an evolutionary standpoint the dorsal region of the body (controlled by the dorsal sensory roots) really ends at the tip of the nose. The area supplied by the ophthalmic branch becomes anatomically a ventral surface only in the primitive primates—*Prosimiæ* [11]—by the anterior expansion of the neopallium. That the ophthalmic branch is in reality a spinal dorsal nerve is shown by its early appearance in the lower vertebrates as a separate nerve and by its connection with the spinal descending root which is present long before the appearance of the principal nucleus of the fifth nerve, the latter not being present in fishes; Brouwer [11] was unable to find any evidence of it.

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11. Brouwer, B.: Die biologische Bedeutung der Dermatomerie Folia Neubrologican, in Woollard: Recent Advances in Anatomy, Philadelphia, P. Blakiston's Son & Company, 1915, vol. 9, pp. 272 and 273.

The principal nucleus of the fifth is first seen in *Amphibia* lying dorsolateral to the motor nucleus. Therefore, in the fish all cutaneous fibers which enter from the head region must run in the descending spinal tract of the fifth nerve. In the selachians, *Dipnoi* and a few of the aquatic amphibians, the ophthalmic branch is separate.[12] Later it becomes joined with the supramaxillary and inframaxillary.

Clinically, the posterior sensory root nature of the ophthalmic branch is shown by the area supplied by it being the frequent seat of true zoster—which but rarely attacks other than the segmental portions of the neurospinal axis.

Anatomic Peculiarities of Ophthalmic Branch.—In man, the ophthalmic branch has a much longer course in Meckel's cave than the second or third branches. It is firmly adherent to the dura of the cave on its under and inner side, and to the cavernous sinus, from both of which it can be separated only with difficulty. Its ganglionic portion lies flat on the dura which is adherent to the bone of the petrous apex and the petrosphenoid articulation mesial to the sector supplying the second and the larger portion going into the third branch. It is slightly above the latter.

On the other hand, the ganglionic fibers of the second and third branches lie on the elastic cushion formed by the internal carotid artery as it runs in the open foramen of the carotid canal. Both the second and third branches enter the cave without adhesion to its dural covering. They also leave the cave anterior to the cancellous tissue of the petrous apex.

Anatomically, then, the ganglionic and peripheral portions of the second and third divisions of the fifth nerve are protected from osseous or dural inflammation, either of which may cause irritation of the ophthalmic portion.

Susceptibility of Ophthalmic Branch to Dural Pulling from Swelling of Bone by an Underlying Suppuration.—Anatomically, the first branch is especially apt to be affected by periosteal swelling as the fibers to the first branch pass over the cellular area of the petrous apex at its junction with the sphenoidal base, where cancellous tissue is apt to be abundant.

But probably it is the "pulling" in the area of its adhesion to the first branch, the result of inflammation of the cancellous tip and petrosphenoid articulation, that gives rise to the extra-ocular pain in the early stages of caries of the petrous apex, as it is doubtful if inflammatory infiltration of the root alone—as occurs in the later stage of abscess formation—will originate pains.

12. Wilder, H. H.: History of the Human Body, New York, Henry Holt & Company, 1923, p. 502.

In Turner's [13] case of sphenoid inflammation with cavernous sinus thrombophlebitis, the patient had no pain behind the eye, although a microscopic inflammatory infiltration of the ophthalmic nerve was demonstrated post mortem. I have had personal experiences of abscess infiltration from thrombophlebitis of the gasserian ganglion without fifth nerve pain.[14]

The freedom from pain in the domain of the third and second branches in petrous apex suppuration is probably due to the fact that they are not subject to dural pulling as they have no dural connection and are in relation with the compact tissue having no cellular elements which form the superior border of the petrous behind and of the carotid artery in front. This type of bone is not apt to transmit inflammatory swelling.

For even in extensive caries involving both the anterior and posterior surfaces of the petrous apex, the compact bone of the superior border remains unaffected (as in cases 1 and 2 of this series), in which case even with extensive destruction of the posterior wall of the petrous apex and a localized meningitis of the bulbar cisterna—associated with stiff neck, nystagmus, sixth nerve palsy with sepsis—there is no facial pain unless the middle fossa is involved by the carious process.

That the characteristic retro-orbital neuralgia is of dura-osseous origin and is not a true neuritis is shown by the fact that in non-suppurative lesions, true trifacial neuralgia—spasmodic tic douloureux—the pain always is spasmodically stabbing—neuralgic—in character, and begins either in the second or third branch but never in the first, although the facial neuralgia involves the first branch at a later date. Again the pain in the supra-orbital or nasal nerves in tic douloureux is never retro-ocular, while the pain of suppurative disease of the petrous apex is cephalalgic (headache)—with a retro-orbital element.

Conclusion.—Consequently, on anatomic grounds and from clinical experience, pain behind the eye may be the first manifestation of congestion or granulation caries of the petrous apex.

(*d*) *Facial Pains in Localized Meningitis.*—If an extradural abscess forms during an infective osteitis, then a neuralgia from direct pressure of any branch of the trifacial nerve may occur (Gradenigo). Such direct pressure is doubtless the cause of the second and third branch pain in cases of exudate into the subdural space of the middle fossa. I have seen one case in which toothache was the result of a brain

13. Turner and Reynolds: Nasal Mucous Polyp; Intranasal Operation on the Ethmoidal Air Cells; Purulent Meningitis, J. Laryng. & Otol. **41**:717 (Nov.) 1926.

14. Eagleton, W. P.: Cavernous Sinus Thrombophlebitis, New York, The Macmillan Company, 1926, case 24, p. 153.

abscess, another of cavernous sinus suppuration [15] and several cases of retro-ocular pain on filling the brain abscess with water,[16] the pathologic lesion being confirmed by autopsy or operation.

Also, I have seen numerous cases of localized meningitis of the base of the middle fossa secondary to bony caries of the external third of the petrous bone which have occasioned headache and pain around the eye, probably from a localized collection of fluid in the middle fossa, as the evacuation of the fluid associated with removal of the carious bone gave immediate relief to the pain.

Value of Lumbar Puncture in Diagnosis and Treatment: Clinically, localized meningitis may be eliminated by the absence of sepsis and an examination of the fluid obtained by lumbar or occipito-atloid puncture. Consequently, it has become my practice before operation on the mastoid to perform lumbar puncture in all cases of facial pain, as the absence of increased pressure and heightened cell count of the fluid adds security to the diagnosis of a nonfatal form of neuralgia.

CLINICAL CONCLUSIONS ON TYPES OF SENSORY NERVE DISTURBANCE ORIGINATING IN OR NEAR THE SUPERIOR SURFACE OF THE PETROUS PYRAMID

There are four distinct types of sensory nerve disturbances which originate in or near the superior surface of the petrous pyramid, all of which are clinically diagnosable during the early stages: (*a*) referred pain from suppurative diseases of the ear, the pain originating from involvement of the communicating fibers of the facial, glossopharyngeal, vagus, and possibly the cervical nerves, and referred to one or other branches of the fifth nerve; evacuation of the mastoid and adjacent cells only is indicated; (*b*) zona—from geniculate ganglion (sympathetic or spinal nerve) involvement—probably from a filtrable virus, a hemorrhagic process associated with herpes; (*c*) true tic douloureux of unknown origin, and (*d*) first branch retro-ocular pain from caries of the petrous apex.

The latter calls for an operative attack on the diseased area.

II. ABDUCTOR PARALYSIS

DIAGNOSTIC SIGNIFICANCE

Dissection on cadavers would demonstrate that sixth nerve paralysis signifies either (1) periosteo-aponeuro-dural swelling in the posterior fossa when it accompanies suppurative disease of the posterior surface

15. Eagleton (footnote 14, case 18).

16. Eagleton, Wells P.: Brain Abscess: Its Surgical Pathology and Operative Treatment, New York, The Macmillan Company, 1922, case 13, pp. 63 and 183.

of the petrous or sphenoid or (2) cerebral displacement in a brain tumor. The suppurative otitic lesions in their earlier stages are extracerebral, whereas a neoplastic process is entirely intracerebral.

ABDUCTOR PARALYSIS FROM DISEASE OF BONE, PERIOSTEUM, APONEUROSIS OR DURA

The Development of Dorello's Canal.—The tissues forming Dorello's canal and Gruber's ligament—viz., (*a*) the periosteum of the bone of the apex of the petrous pyramid and the occipitosphenoidal base, with (*b*) the dural covering and (*c*) the aponeurosis of the petro-occipital articulation and the petrosphenoidal ligament uniting them—are developmentally one structure, inseparable from one another. They are all of mesoblastic origin, all modifications of fibrous tissue and all have one purpose, viz., the protection of the central nervous system from injury by trauma or infection. It is the intimate relationship with the mesoblastic tissue surrounding the sixth nerve which makes it especially liable to pressure in inflammation of the periosteum, dura or aponeurosis.

Resemblance Between Sixth and Seventh Nerves.—Anatomically, the sixth nerve has many points of similarity to the seventh—also a motor nerve. Like the facial nerve it is also frequently paralyzed in local suppurative disease and in fractures of the cranial base.

The sixth nerve as it leaves the pontile cisterna and enters Dorello's canal immediately loses its arachnoid covering, as does the facial nerve on entering the fallopian canal. The fifth nerve, on the other hand (largely sensory), has a free passage through a large tentorial ring, is surrounded by loose arachnoid prolongations and is bathed in cerebrospinal fluid.

Neither the facial nor the sixth nerve has a neural sheath from the time of its entrance into the respective canals until the exit—at the stylomastoid foramen [17] and from the cavernous sinus, respectively.

Consequently, any pressure, be it inflammatory or traumatic, of the tissue forming the canals of the sixth and seventh nerves (aponeurodural in the case of the sixth, bony in the facial) will paralyze either the abductor or the facial nerve.

Sixth Nerve Paralysis That Disappears After Mastoid Operation.—(See appendix.) My dissections in Paris established the bizarre character of Dorello's canal as regards its position, size, shape and anatomic formation as would necessarily result from the nature of its development, its position, size, shape and structure being determined by the configuration and symmetry of the bony base—a very irregular and

17. Ballance, Charles; and Colledge, L.: Anatomic Observations of Nerves of Face and Neck, J. Laryng. & Otol. **42**:1 (Jan.) 1927.

asymmetrical body. Consequently, the canal does not conform to any standard of length, diameter or circumference of lumen.

Even the nerve itself presents variations very unusual in the nervous system, as it is frequently double, with great variations in size or length.

ANATOMIC FACTORS INFLUENCING THE LIABILITY TO ABDUCTOR PARALYSIS IN DIFFERENT PATIENTS

Among the anatomic factors influencing the liability of different patients to abductor paralysis are:

(*a*) The differences in the length of the nerve in the dural canal, varying greatly as it does (see table).

(*b*) Its anatomic position on the bony basis (whether on the bone or on the articulating surface of the petrobasilar suture).

(*c*) The extent of the closure of the articulation between the petrous apex and the occipital and sphenoidal base, which is among the last of the cranial sutures to undergo complete ossification; consequently, the younger the patient, the more extensive the aponeurotic fibers and the greater liability to transmission of dural inflammation by septic swelling. This may partially explain the greater frequency of abductor paralysis during the early decades.

(*d*) The closeness of its attachment to the periosteum. In this respect the sixth nerve is even more liable to paralysis than the facial nerve, as there are no fibrous connections between the bone and the facial nerve, which can be easily lifted out from its canal up to the point of its exit from the stylomastoid foramen, while the sixth nerve in its whole course through Dorello's canal is united either tightly, or loosely, by connective tissue fibers with the periosteum, the aponeurosis, Gruber's ligament or the dural covering.

(*e*) The great variation of the size of the nerve and its freedom in the canal. At times the nerve is tightly constricted and immobilized by the dura and the periosteum—as is the facial by the bone—and again it is moderately loose, allowing of considerable motion when pulled upon.

All the foregoing factors may influence the liability to abductor paralysis not only of the homolateral but of the contralateral side.

Thus swelling of any of the surrounding dura or aponeurosis may furnish pressure enough to paralyze the nerve even without inflammatory change in the bone itself. The latter is the direct paralyzing factor in the majority of the cases, as well as the underlying cause in all. Thus with a long dural course and a closely attached canal, slight inflammation of the periosteum or dura would cause paralysis of the sixth nerve. It is conceivable that a "rheumatic" toxic swelling of the

fibrous bands (tendinitis) of the articulation could cause sufficient pressure to paralyze a tightly held nerve.

PARALYSIS FROM NEURITIS OF NERVE ITSELF

Pathologic evidence suggests that the sixth nerve only undergoes degenerative neuritis from pressure of the surrounding structures and is not paralyzed by changes of temperature as occurs in the facial nerve, the sixth being a pure motor nerve while the facial in the lower vertebrate is a mixed motor and sensory nerve and even in man contains sensory fibers, and thus is probably susceptible to the stimulus of changes in temperatures. Toxic agents such as diphtheria are frequently the cause of an abductor paralysis, the result of a peripheral neuritis.

Relation with Inferior Petrosal and Its Communications.—In its ascent on the posterior surface of the bone or on the articulation, the sixth nerve may be in relation with the plexus of veins emptying into the inferior petrosal sinus.

OSSEOUS FACTORS IN THE PRODUCTION OF ABDUCTOR PARALYSIS

It is the character of the bone itself that decides whether the nerve will be paralyzed or not, depending on whether the bone structure is adapted to the transmission from a distance of congesting swelling, viz., whether or not the osseous structure of the petrous apex has an underlying cellular or spongy structure. A pneumatic bony structure with cells extending from the middle ear to the petrous apex, is especially liable to the development of abductor paralysis. These are the cases in which recovery results after simple opening of the mastoid. The nature of the osseous structure is of special importance in those cases in which the nerve passes under the petrous spine. Here one of the abducens nerves may be almost completely surrounded by cellular bone, while that of the opposite side is entirely free of bony contact, as occurred in one cadaver. In such a case it is conceivable that slight swelling of the periosteum, sufficient to paralyze the abductor of the side contralateral to the suppurating ear, might be transmitted across the base to the contralateral nerve while that of its fellow may escape. This may be the explanation for some of the cases of contralateral abduction paralysis that have disappeared after a simple mastoid operation.

At the superior border of the petrous the sixth nerve may be subject to pressure from the petrosphenoid (Gruber's) ligament which, like all the other mesoblastic structures of this region, varies greatly, as Gruber's ligament is only a part of the aponeurotic fibers uniting the

petrous with the mesial base. The direction of the fibers composing the ligament—from vertical to horizontal—dictates the size of the underlying canal, which may vary from a large canal in which the nerve lies free, to a very small canal sending attachments to the nerve or even dividing the nerve into two portions.

RELATION OF ABDUCENS TO THE SPHENOID

Internal to the spine of the petrous apex, the sixth nerve may come in intimate relationship with the sphenoidal sinus, and when the sphenoidal body is diploic, the nerve may be separated from the mucous membrane of the sinus simply by a thin layer of compact bone. This applies not only to the sinus of the homolateral, but occasionally to that of the contralateral, side; this occurred in one cadaver in which an edematous swelling of the mucous membrane of the right sphenoidal sinus might have caused an opposite (left) abductor paralysis, as a posterior prolongation from the right sphenoid passed behind the left sinus and extended to the opposite petrous spine.

RELATION WITH VEINS OF PERITUBAL REGION AND ABDUCTOR PARALYSIS OF VENOUS ORIGIN

The abducens come into relationship with the plexus of veins which run from the anterior part of the inner wall of the tympanic cavity, through the bone of the petrous pyramid—peritubal region—to the cells of the petrous apex (Pietratoni). A microscopic thrombophlebitis of these veins in the presence of a cellular bony apex might give rise to abducens paralysis.

ABDUCTOR PARALYSIS FROM INTERMENINGEAL SUPPURATION

In the early stages of a suppurative otitis it is the intradural or periosteal inflammation which causes abductor paralysis. However, when the pontile cisterna is the seat of an adhesive exudate from localized or general suppurative bulbar meningitis, the nerve may be paralyzed from the arachnoid inflammation itself.

I have seen an abductor paralysis associated with a low grade of papilledema which disappeared on evacuating an excess of cerebrospinal fluid by a lumbar puncture (M. L., case [18]). Contrary to the

18. M. L.: Case Report.—Following mastoid operation, a boy had pain behind the ears and eyes; he developed external homolateral rectus paralysis and a papilledema. Lumbar puncture showed apparently clear fluid; increased pressure; cell count, 7; coagulable albumin, a trace of chlorides, 0.71 and no micro-organisms. Second lumbar puncture a few days later showed: clear fluid; still slightly increased pressure; increased trace of coagulable albumin; cell count, 5; lymphocytes; chlorides 0.16 and no increase in globulin. Following this puncture there was a rapid subsidence of the papilledema.

generally accepted view, abductor paralysis is rarely the result of leptomeningeal inflammation—except as a terminal process—as shown by its absence in three of the four cases of bulbar meningitis, in all of which suppurative meningitis must have surrounded the nerve for a considerable period as demonstrated by autopsy. In the one case in which abductor paralysis was present it was manifestly a terminal process.

Anatomically, the liability to paralysis from suppurative intra-arachnoid inflammation—localized or general suppurative or serous meningitis—is dictated by the (*a*) length of the nerve on the anterior surface of the pons (in the pontile cisterna) and (*b*) by the position, axis and size of the entrance of Dorello's canal, all of which conditions vary greatly in different cadavers, and on the two sides in the same cadaver. There is a small group of cases in which lumbar puncture causes a prompt disappearance of the symptoms, the lesion apparently being a nerve congestion from irritation of an overlying infective ostitis.[18]

III. LOCALIZED BULBAR CISTERNA PONTILE MENINGITIS

ANATOMIC PORTION

As clinical experience has taught that (1) the site of the primary focus of osteitis or phlebitis determines where the infection enters the arachnoid, and as postmortem examinations have demonstrated that (2) the course which the meningeal inflammation takes after passing the dura is largely dictated by the normal channels in the arachnoid meshes with their connections into the cisterna (similar, to a certain extent, to the course that a phlebitis must take in a large venous sinus following its lumen and connections), and as there is postmortem and clinical evidence that in all types of meningitis nature makes an effort to limit the disease, it would appear reasonable to assume that if a diagnosis can be made of the exact site of the infection while it is limited to a particular area—be it the cisterna of the angle or of the bulb—cure from surgery should be obtained in a considerable proportion of cases of meningitis, as in cases of empyema of the ductus endolymphaticus and of the internal auditory meatus. Consequently, an effort was made to ascertain the direction in which otitic suppurative meningitis should advance in the meshes of the arachnoid of the posterior fossa, if such advance is dictated by the anatomic formation of the spaces.

A succession of cadaver "heads" arterially injected were dissected, in which a dye had been allowed to diffuse (*a*) from the labyrinth into the subarachnoid spaces surrounding the internal auditory meatus and (*b*) from the region of the jugular bulb; two areas, which when attacked by suppurative disease, frequently give rise to meningitis.

EXPERIMENTAL PORTION

For surgical reasons, the posterior fossa may be divided into an anterior and a posterior compartment. The line of division is the arachnoid prolongation surrounding the nerves leaving the brain.

Anatomically, there can be distinguished the following sites, from which a carious process of the posterior surface of the petrous bone may cause a localized meningitis of the posterior fossa by extension through an arachnoid prolongation: (*a*) in the region of the ductus endolymphaticus, (*b*) through the prolongation surrounding the internal auditory meatus, (*c*) in the cisterna of the angle, and (*d*) of the bulbar cisterna; (*e*) by way of an unnamed prolongation to the superior border of the petrous, internal to and above the internal auditory meatus (possibly the arachnoid surrounding the remains of the structure entering the fossa subarcuata and (*f*) by way of the region through which the ninth, tenth and eleventh nerves pass out of the anterior compartment of the jugular fossa.

The diffusion by gravity of dye when placed in the meshes of the arachnoid connected with the labyrinth and the lateral sinus—both the frequent cause of septic leptomeningitis—furnishes (1) a graphic map of the region that infection will take as dictated by the anatomy of the arachnoid pathway, and (2) the points at which the infection can easily be limited by adhesions.

Dye in solution placed in an arachnoid prolongation, after passing into a cisterna, diffuses into the other prolongations of the cisterna, but the communication of the arachnoid prolongation pathways of the posterior fossa from the cisterna are so small that particles of dye in suspension may be prevented from reaching the cisterna in many localities, although dye in solution passes freely. This shows the ease with which different areas of arachnoid may be walled off, and infection thus limited by inflammatory reaction.

1. Dye introduced into the arachnoid prolongation surrounding the internal auditory meatus has a tendency to go (*a*) forward and upward into the middle fossa by way of the third nerve region; (*b*) around the superior collar of the cerebellum, and (*c*) downward along the anterior surface of the medulla and cord, without entering, to any great extent, the pontile cisterna itself. This latter area is apparently protected by (1) the close mesh of the arachnoid, (2) the latter's adhesions to the basilar artery, and (3) the arachnoid's flat position on the bony base.

2. Dye placed around the jugular bulb has a tendency to diffuse backward under the cerebellum and down the posterior surface of the cord—the posterior compartment.

3. Dorello's canal surrounding the sixth nerve does not admit any dye.

4. Dye in the prolongation of the fifth nerve extends halfway across the floor of the middle fossa.

SYNOPSIS ON CLINICAL PORTION

Two cases of caries of the petrous apex from suppurative otitis are reported, both presenting the suggestive "pain behind the eye," associated with a low grade of chronic sepsis and recurrent attacks of slightly stiff neck.

In one case these prodromal signs lasted sixteen days and in the other forty-three days before the onset of symptoms of bulbar cisterna meningitis. The symptoms of bulbar cisterna meningitis I believe are pathognomonic, viz.: (*a*) semicoma from which the patient can easily be aroused; (*b*) supine position of the patient (on back) with the eyes closed and (*c*) intermittent recurrences of vertical nystagmus.

All signs of posterior fossa involvement so usual in severe headache, great restlessness and opisthotonos but unaccompanied by cortical meningitis, were associated with a high fever and rapid pulse. Repeated trials of visual fields revealed great bilateral variations and the sudden appearance of a bitemporal hemianopsia somewhat resembling pituitary tumor pressure.

The fluid from the lumbar region was cloudy, but contained no organisms. Autopsy in both cases disclosed a large carious cavity involving the petrous apex and extending onto the anterior and posterior surfaces of the petrous pyramid, causing a localized meningitis of the pontile cisterna followed by a general suppurative meningitis as a terminal process.

The anatomic location of the focus of suppuration explained the clinical symptoms of fifth nerve pain and bulbar cisterna infection—a combination of middle and posterior fossa symptoms with extension into the chiasmal cisterna.

Two additional cases of bulbar meningitis of traumatic origin are also reported, a clinical diagnosis of bulbar meningitis having been made during life because both patients presented similar clinical pictures without primary middle fossa involvement.

Autopsies confirmed the diagnosis that the meningeal process in the early stage was confined to the bulbar cisterna.

REPORT OF CASES

CASE 1.—*Pontile Cisterna Meningitis the Result of Caries of the Petrous Apex Which Also Produced Secondary Labyrinthitis.*

History.—J. McE., a man, on March 5, following an attack of influenza, had a right-sided earache followed by a profuse discharge which continued until March 15, when the otorrhea lessened. During this time he had a slight rise in

temperature, complained of headache, pain behind the eye and severe pain in the right side of the face and jaw extending back to the right ear, all of which he attributed to neuralgia.

March 16: Dr. J. J. Mann found a moderate discharge from the ear with a slight drooping of the posterior-superior wall and a little tenderness over the antrum. The temperature was 102 F. A roentgenogram showed that the antrum alone was involved. The next day the symptoms had improved, but the tenderness had lessened. During the following ten days the patient did not return to Dr. Mann, as he continued to improve, although at times he had "neuralgia" pains in and over his eyes and in his temple.

March 28: After passing several restless nights, he suddenly developed a facial paralysis on the right side and total deafness in his right ear, associated with spontaneous nystagmus and unsteadiness of gait. He was sent by Dr. Mann to the Newark Eye and Ear Infirmary. The chief complaint was facial paralysis followed by pain in the right eye for the previous ten or twelve days.

Examination.—The patient was right-handed. He did not look sick but had the whitish appearance of chronic nephritis. There was a slight aural discharge, with right-sided facial paralysis and deafness, and spontaneous nystagmus to the left (away from the suppurating ear).

The right pupil was smaller than the left, which was explained by the patient who said that the vision of the right eye had never been as good as the left. The right cornea was sensitive, but apparently less so than the left. The disk margins of the right eye were blurred, and the vessels were engorged. The visual field suggested a bitemporal indentation. The temperature was 99 F. and the pulse rate 80.

On lumbar puncture the fluid was not under pressure, and was clear (5 cells per cubic millimeter); it contained a trace of albumin; the globulin was not increased; the sugar reduction was normal, and the chloride content was 0.67. Urinalysis revealed; specific gravity, 0.20; albumin, 1 plus; granular casts, 3 plus; squamous epithelium, 1 plus; pus cells, 3 plus; red blood cells, 2 plus. The blood pressure was 140.

Diagnosis.—"Acute labyrinthitis with involvement of the horizontal semicircular canal from subacute otitis media."

It was decided (chiefly because the negative cerebrospinal fluid changes apparently denoted an absence of meningeal involvement) to allow time for the labyrinthine lesion to become fully localized.

March 29 to 30: The patient apparently was in excellent condition. Nystagmus was lessened. There was no pain in the head, but once during the night he felt pain in the right eye (to which proper attention was still not paid). The temperature varied from 98.3 to 99.4 F.; the pulse rate, from 72 to 88.

March 30: The patient passed a bad night. He complained of severe pain over the right eye, and his temperature reached 101 F. The following morning, however, the temperature was 100 F. and the pulse rate 80, and the pain in the eye had lessened considerably. Slight rigidity of the neck was now noted for the first time.

Preoperative Diagnosis.—"Acute non-suppurative labyrinthitis with a probable erosion of the external semicircular canal, associated with a localized meningitis, the result of congestion of the cells under the trifacial, the latter probably secondary to invasion of the perilabyrinthine cells."

Comment.—The mistake was made of not appreciating that an acute labyrinthitis which had followed a period of retro-ocular pain was at least suggestive

of infection of the labyrinth secondary to suppuration of the apex of the petrous, rather than extension from the antrum.

Operation.—The mastoid was opened; pus and granulation were found in the cells and antrum. The external arm of the horizontal canal was eroded and replaced by granulation tissue. The solid angle was removed, as well as the cells behind and above the horizontal canal. The posterior semicircular canal was exposed, just behind which, from the region of the ductus endolymphaticus, a drop of pus was evacuated. A small opening in the dura of this region liberated a considerable quantity of cerebrospinal fluid from which *Streptococcus non-hemolyticus* was cultivated.

Comment.—I did not explore the gasserian ganglion region of the middle fossa because in a rather large experience of cases with irritation of the branches of the fifth, evacuation of the cerebrospinal fluid from the middle fossa had been followed by relief. Not sufficient attention was paid to the persistence of localized pain behind the eye, in the face and temple, suggesting, as it did, a definite lesion of the petrous apex. But as the operative observations were felt to warrant the preoperative diagnosis, I expected the man to recover, although one of my associates called attention to the presence of the nystagmus, which was now toward the side of the lesion, as suggestive of a brain stem involvement.

Postoperative Course.—The patient had no more than the usual postoperative discomfort during the first night; he slept irregularly. The temperature was around 101 F. On the following day (April 1), however, his temperature became elevated and continued from 103.3 to 104.4 F.; he suffered from incontinence and had a stiff neck; he developed a peculiar type of stupor, that is, although he lay continuously flat on his back with his eyes closed and head retracted, on being spoken to he would immediately open his eyes and promptly answer questions, stating that he did not feel "so good."

The patient now, although manifestly suffering from meningitis—as in addition to the stiff neck he had an internal strabismus—(from complete paralysis of the right external rectus) and a vertical nystagmus, there was an entire absence of the usual meningeal restlessness, headache and screaming.

The intra-ocular tension was very low in both eyes (10 mm. of mercury, Schiotz), which probably was due to the loss of cerebrospinal fluid on the previous day.

A second lumbar puncture revealed turbid fluid, with a white cell count of 4,000, a red cell count of 1,200, globulin and no micro-organisms.

Diagnosis.—A diagnosis was made of acute fulminating suppurative meningitis of the lateral prolongation of the pontile cisterna from extension through the modiolus, secondary to suppurative labyrinthitis.

NOTE: The vertical nystagmus was explained by the supposition of an injury to the cerebellum associated with the previous operation.

Second Operation.—With the patient under local anesthesia the common carotid was ligated without occasioning any circulatory disturbance. The vestibule of the labyrinth was opened from behind by throwing the posterior arm of the horizontal canal and the posterior vertical semicircular canal together. There was no pus in the vestibule but possibly a little blood. The cochlear was opened from the middle ear through the promontory but was found empty. Pia-arachnoid prolongation surrounding the internal auditory meatus was incised from behind the pyramid and a large quantity of cerebrospinal fluid evacuated. The middle fossa was not opened because of the outstanding posterior fossa symptoms, viz., vertical nystagmus, sixth nerve paralysis, stiff neck and retraction of head completely filled the clinical picture.

Subsequent History.—April 2: The patient continued to be in a semicomatose state, with continuously high temperature and rapid pulse, but could be easily aroused. He gave the impression of being in nephritic coma, as he had little of the restlessness or the crying out of meningitis. There was lateral deviation of the eyes to the right and upward. The vertical nystagmus disappeared but recurred on the following day. Lumbar puncture now revealed streptococci.

After-Treatment.—Repeated lumbar punctures were made associated with blood transfusions.

April 4: The patient died of terminal pneumonia.

Postmortem Examination.—The petrous apex was the seat of a carious process which had eroded both the anterior and posterior surfaces of the pyramid, but with the compact bone of the superior border of the petrous tip still remaining. The area of caries was about two thirds of an inch long and one third of an inch wide on the floor of the middle fossa, and slightly smaller on the anterior wall of the posterior fossa. The cavity in the bone was much deeper than appeared externally; the cavity undermined the internal auditory meatus extending below and anterior to it. Mesially, the carious process reached the petroso-occipito-sphenoidal suture. The bony cavity was filled with granulation tissue and pus. On the anterior surface, the granulations were compressed and held flat by the dura covering it. It gave the usual appearance of granulation tissue which had been held under pressure for some time. On the anterior surface of the petrous the fossa of the gasserian ganglion was involved, the ganglion itself being edematous. The outer surface of the dura covering the gasserian ganglion was hemorrhagic.

On the posterior surface of the petrous, the granulation tissue spread beyond the level of the bone and was here covered with pus.

Meninges: There was practically no meningitis of the cortex, but a little meningitis confined to the bulbar cisterna (over the pons and medulla as it lies on the occipital process below the posterior clinoid process).

Brain: The basal ganglion (optic thalamus) of both sides appeared blackened and degenerated as if containing multiple hemorrhages. There was no internal hydrocephalus but moderate distention of the third ventricle.

CASE 2.—*Localized Caries of Apex of Petrous Pyramid Without Labyrinthitis; the Route of Invasion Having Been Through the Supratubal Cells, and Associated with a Chronic Meningitis of the Bulbar Cisterna, the Latter Existing for a Considerable Period Before Becoming General.*

History.—A. R., a young woman had acute right-sided otitis five years before examination. On Dec. 8, 1926, she had pain in the right side of the head, and a discharge from the right ear, accompanied by vomiting.

December 18: She was admitted to the Newark Eye and Ear Infirmary on the service of Dr. John Hemsath, with a diagnosis of acute right-sided mastoiditis. The temperature varied from 99.3 to 101.1 F.

December 20: A simple mastoid operation was performed. Pus and granulations were found in antrum and mastoid cells. A culture from a smear from the mastoid showed *Streptococcus nonhemolyticus.* The patient was discharged six days later apparently in excellent condition.

Jan. 4, 1927: She was readmitted to hospital complaining of irregular pain in the head and general malaise, with profuse discharge from the mastoid wound and ear. The temperature and pulse were normal. She remained in the hospital until January 28, during which time she had several attacks of rather severe pain in the head which were relieved by dressing of the wound. On January 13, she

complained of slight dizziness, in addition to the headache. The former disappeared and did not return, but the headaches persisted irregularly, at times being almost entirely absent and again severe. The temperature varied between 98.3 and 100.3 F., but on one occasion it reached 101 F., and on another 102 F. The visual fields were suggestive of bitemporal hemianopic contraction.

January 14: The patient complained of a stiff neck accompanying her headache. The visual field was suggestive of right-sided hemianopic indentation. A few days later (January 18) the visual field was suggestive of left-sided hemianopic indentation.

January 22: The patient cried with a severe pain on the right side of her face.

Repeated blood counts showed: erythrocytes, 4,800,000; hemoglobin, 85 per cent; leukocytes, from 9,200 to 8,400; polymorphonuclears, 78 to 80 per cent; lymphocytes, from 20 to 22 per cent. Cultures were negative. The Wassermann reaction was negative.

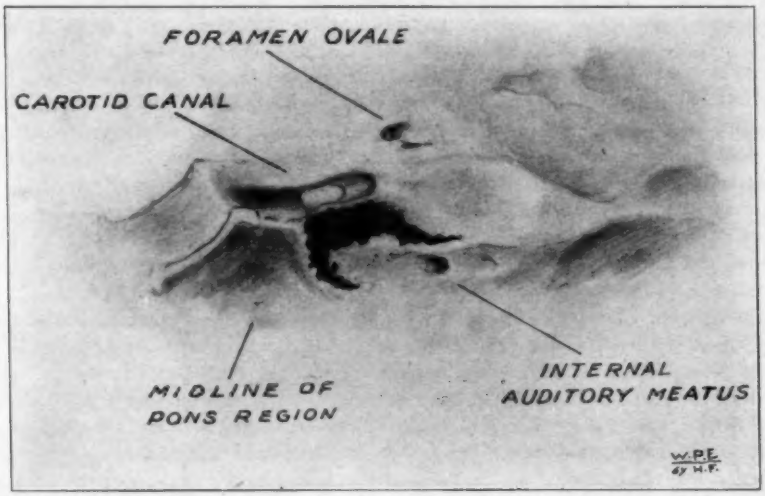

Fig. 1 (case 1).—Caries of the petrous apex showing erosion on the superior surface.

February 8: The patient had considerable pain over the right eye, the pain in the head now being definitely located in this region. She also had severe dizziness and pain in the back of the neck. The temperature varied from 99 to 102 F. The visual fields were suggestive of a bitemporal hemianopic indentation.

February 18: The patient was transferred to the Cranial Surgery Department, with the statement that "during the past ten days the patient has had attacks of pain in the head and over the right eye; a slight stiff neck, and an irregular temperature, 100 to 101 F., and that on the previous night she had had an attack of severe dizziness, associated with nystagmus and vomiting."

The temperature suddenly rose to 106 F., and the pulse rate to 120. The patient was now complaining of severe pain in the left side of the head. The neck was markedly stiff.

Examination.—There was spontaneous horizontal nystagmus to the right, with a tendency to divergence. The disk margins of the right eye were slightly indis-

tinct; the vessels were full, tortuous and dark. Hearing on the affected side was present, but reduced. There was weakness of the left lower side of the face (opposite to the side of the suppurating ear). The tongue protruded in the midline. All reflexes were diminished. The blood count showed: leukocytes, 16,000; polymorphonuclears, 86 per cent; lymphocytes, 14 per cent.

Lumbar puncture showed a pressure of 20 mm. of mercury; cloudy fluid, 3,500 cells per cubic millimeter, chiefly polymorphonuclear; coagulable albumin; slightly increased globulin; chloride content, 0.63 and no micro-organisms.

Roentgen examination showed: moderate cloudiness of the right frontal sinus and the right ethmoids.

The visual fields showed marked bitemporal contraction of both fields.

Diagnostic Impression.—The diagnostic impression was: "right cerebellar abscess with secondary meningitis. Of course, the fact that she had severe pain in her eye would make it look as if the middle fossa was affected, but the marked nystagmus puts the infection in the posterior fossa. It may be that she has a meningitis of the whole of the base, causing the nystagmus."

Third Operation.—The right common carotid was ligated. The solid angle was removed, the lateral arm of the right cisterna pontis opened, and a large quantity of fluid evacuated. An explorative puncture of the cerebellum for abscess was negative. Puncture of temporal lobes also revealed negative results; in the performance of the puncture a distended right lateral ventricle was tapped.

Death resulted in coma from meningitis four days after operation.

The lumbar fluid remained sterile until the day prior to death, when it contained streptococci.

Postmortem Examination.—On removal of the dura from the right petrous bone, the apex was seen to be the seat of a cavity. Into this cavity a probe could be passed the distance of two thirds of an inch. It involved both the anterior and the posterior surfaces of the petrous pyramid with the compact bone of the superior border of the petrous remaining. The cavity was filled with semisolid yellowish material, which looked like cholesteatoma. The mass was apparently held in shape by the overlying dura. On the anterior surface of the pyramid, the carious area lay under the fifth nerve, the overlying ganglion being edematous and surrounded by granulation tissue. The purulent granulomatous mass included the carotid canal, although the carotid artery was pervious. The adjacent cavernous sinus was apparently obliterated, for its cavities could not be found; however, it did not contain pus. The posterior surface of the petrous apex was also eroded; the orifice of the cavity on this surface extended from the petro-spheno-occipital suture mesially to within one-third inch of the inner border of the internal auditory meatus; the latter in its depth was undermined by the carious cavity. The pathologic cavity was one-half inch in width, three-eighths inch in length and three-eighths inch in the vertical plane. It contained a mass of cheesy pus and detritus which resembled cholesteatoma.

Comment.—The location of the cavity, involving both the anterior surface of the petrous (that is, the floor of the middle fossa) and the anterior wall of the bulbar depression in the posterior fossa, explained the combination of symptoms of gasserian ganglion pain and marked nystagmus of bulbar origin.

Postmortem Examination of Meninges.—From the bony focus there had originated a meningitis of the bulbar cisterna, which latter was the site of a purulent exudate. This exudate extended from the pontile region forward to the chiasmal cisterna and laterally the process had broken loose from the bulbar

cisterna, where it had been confined for a considerable period, spreading, as it did, from the bulbar cisterna forward into the chiasma and laterally over the cerebellum.

The terminal diffuse meningitis was only a sequela of the localized meningitis of the bulbar cisterna.

The distinct limitation of the carious process as found post mortem warranted the belief that the case offered a good prospect for recovery had the condition been diagnosed early and radical operation been performed with drainage of the infected bony area along the floor of the middle fossa. And even at a much later period (when the dizziness and stiff neck gave warning that the posterior fossa was affected), the localization of the meningitis to the bulbar cisterna, which had resulted from a slow localized caries, showed that the septic processes were still controllable if a radical attack on the carious area even then had been associated with evacuation of the fluid in the bulbar cisterna.

Comment on Cases 1 and 2.—Both cases 1 and 2 contain distinct aspects of similarity which should have allowed an early diagnosis of (1) caries of the petrous tip, and later (2) of meningitis of the bulbar cisterna, the latter condition invariably resulting from the former when unrelieved by surgical intervention. As a result of these two pathologic processes both cases presented (3) a symptom-complex of middle fossa and posterior fossa (bulbar cisterna) involvement, and this in chronologic order.

(1) Symptoms of Caries of the Petrous Apex (Middle Fossa Symptoms): Both patients had pain referred to the first branch of the trifacial nerve for a considerable period of time before meningitis became outstanding. In A. R., the pain lasted from January 22 to February 18 (twenty-six days); in J. MacE., from March 15 to April 1 (fifteen days).

The pain in the face and teeth probably was due to involvement by the carious process of branches to the sensory root, and of the dura, which is very adherent to the bone largely because of the passage of fibers of Arnold's nerve with the great superficial petrosal in the hiatus fallopii.

Dissection on cadavers has shown me that the nerve connection which passes under the gasserian ganglion cannot be separated easily from the bone, although extradural and on the surface of the bone itself.

The retro-ocular pain—pain behind the eye—was referable to an involvement by edema or inflammatory infiltration of the dura itself, with a pulling on the first branch, as in both cases. At postmortem examination, "the outer surface of the dura of the gasserian region was more or less hemorrhagic."

(2) Symptoms of Bulbar Cisterna Meningitis (Posterior Fossa Symptoms): (*a*) Both patients had early stiff neck associated with (*b*) subacute sepsis, viz., general malaise, headaches, restlessness at night and irregular slight temperature in the presence of an otitis. This slight stiff neck was the first manifestation of an involvement of the carious process into the bulbar cisterna of the posterior fossa. This meningeal lesion which, for a considerable period, remained localized ultimately presented a symptom-complex, which I believe to be diagnostic of bulbar cisterna meningitis.

(*c*) There was nystagmus of brain stem origin, viz., at first toward the side of the lesion and later vertical in direction, associated with (*d*) a stupor, which resembled the stupor of cerebellar abscess—accompanied by stiff neck—little headache, high temperature, high cell count of the sterile fluid from the lumbar region, but unassociated with the violent headache, restlessness and delirium of cortical meningitis.

This bulbar cisterna meningitis, after remaining localized for a variable time, spreads forward and may cause (*e*) a bitemporal contraction of the visual fields, which was present in both cases and may be of the greatest diagnostic importance.

(3) Other Points of Similarity in the Two Cases: Both cases showed a hemorrhagic process in the basal ganglion of the brain; concerning the origin and significance of this I have nothing to offer.

Both cases showed absence of the sixth nerve involvement until the period of terminal meningitis.

Neither case showed an internal hydrocephalus so frequently present in the usual cases of meningitis of the posterior part of the base.

CASE 3.—*Fracture of Cribriform Plate of Ethmoid and Pneumococcic Meningitis of the Bulbar Cisterna.*

History.—One week before examination, a child fell, hitting his head against a stone and receiving a small cut on the right side of the nose. The wound became infected. The patient became feverish and restless. Three days later he began to have severe headache and stiff neck, followed by difficulty with speech and semiconsciousness. He was brought to the City Hospital on the seventh day after injury.

Examination.—The patient lay quietly in a semicomatose condition, from which he could be aroused. He was irrational at times, however. The temperature was 104 F. The pulse rate was fast and variable. The frontal region showed a small hematoma (and a burn from the use of a strong liniment which had been applied to relieve his headache).

Eyes: There was a small laceration of the skin over the lacrimal region of the inner side of the right orbit, but no discharge. There was no ecchymosis of the lids or conjunctiva; the pupils were equal, and reacted to light and in accommodation, but had a spontaneous horizontal nystagmus which became vertical on looking upward. Hearing was present in both ears; there was no bleeding.

There was marked rigidity of the neck, which the father said had been present for three days. A marked Kernig sign was seen on the left side; it was slight on the right. The knee jerks were active. The Brudzinski sign was positive, the cremasteric reflex positive, and the abdominal reflexes absent. A roentgenogram for fracture of the cribriform plate was negative.

On lumbar puncture the fluid was found under marked pressure; it was clear and contained but 392 cells per cubic millimeter and pneumococci (gram-positive diplococci).

Diagnostic Impression.—The diagnostic impression was: "From the horizontal and the vertical nystagmus (brain stem); the retracted position of the head, and especially from the fact that he has not the meningeal cry, but lies in a stupor from which he can be aroused, I am of the opinion that the patient has an involvement of the cisterna of the brain stem, that is, over the pons."

Suggested Treatment.—Because of the similarity of the clinical picture to patients A. R. and MacE. (cases 2 and 1) who had definite lesions in the bulbar cisterna, I removed the child to the Eye and Ear Infirmary, with the idea of washing out the bulbar cisterna by the introduction of a cannula passed through the inner side of the orbit and then intradurally along the lateral wall of the cavernous sinus and continued through the subarachnoid prolongation of the fifth nerve, thus opening into the basal cisterna, which latter at this point extends a considerable distance anterior to the plane of the pons. Although I had practiced this puncture on several cadavers (sometimes without puncturing the cav-

ernous and again entering either it or the middle fossa), when it came to performing it on a living patient I was reluctant to submit him to the risk.

Treatment.—Occipito-atloid puncture was performed. The fluid at first was slightly bloody but soon became clear; it contained no cells but numerous pneumococci.

Subsequent History.—The patient continued in unconscious state with occasional periods of restlessness, high temperature and rapid pulse.

Lumbar puncture showed fluid under pressure; it was cloudy, straw-colored and contained pneumococci.

Postmortem Examination.—A small fracture was seen through the posterior portion of the cribriform plate. There was no hemorrhage into the orbit, but a small spot of ecchymosis into the brain cortex over the site of the fracture. The meninges of the base of the brain showed exudate in a typical ring surrounding the brain stem, which was distinctly marked and outlined by the limited exudate (fig. 2). The upper part of the cord was also surrounded by a thick exudate.

In addition to this exudate around the brain stem, there was a thick exudate in both the ventricles so that it could be readily wiped away. (Whether this shows that the infection was primary only in the ventricles and then passed into the brain stem, I do not know; but I think it was the other way about; viz., that it went from the brain stem into the ventricles.)

While there were a few spots of exudate in the cortex, nearly all were situated beside the longitudinal sinus, showing how nature was making an effort to eliminate the infection by carrying the exudate into the veins themselves, and that the venous congestion so usual in cases of meningitis is a protective process of nature.

The tract of cerebral injury did not seem to go into the ventricle, although there were also little spots of ecchymosis in the brain.

The convolutions were obliterated, showing that the internal hydrocephalus in these cases was probably due to ventricular exudate.

(At the completion of the postmortem examination, I passed a probe through the opening near the lacrimal sac backward, and entered the gasserian ganglion. I probably could have washed through the infected bulbar cisterna by means of one cannula introduced by this route and another cannula in the occipito-atloid region.)

Comment.—It would seem from this case that the washing out of the base by Van Allen's method, and possibly the washing out of the ventricles (for the brain was under great tension) is feasible in certain cases.

CASE 4.—*Bulbar Cisterna Meningitis. Infection Entering the Arachnoid from Below by Way of the Pharyngeal Plexus Following an Infected Wound of the Posterior Pharyngeal Wall and a Fracture of the Anterior Part of the Body of the Cervical Vertebrae.*

History.—On September 30, the patient was shot, the bullet from a large revolver passing through the left molar region and driving a tooth in front of it which lodged in the mucous membrane of the soft palate. After traversing the base of the tongue, the bullet perforated the posterior pharyngeal wall and lodged in the soft tissues of the opposite side of the neck. On admission to the hospital, the patient was conscious, complained of pain on the right side of the neck which was somewhat swollen. He was expectorating considerable blood. A large lacerated wound of the palate, tongue and nasopharynx, made by the bullet, could be distinctly seen.

During the next few days, the temperature varied from 100.4 to 102.3 F., but on October 6 rose to 104.5 F. The stiff neck was thought to be due to the suppurating wound. The bullet discharged spontaneously into the nasopharynx.

The patient was fed by stomach tube and was given aseptic lavages to combat infection.

October 7: There was an high irregular temperature varying from 105 to 102 F., accompanied by several chills and sweats. The blood cultures were negative. The leukocytosis was 18,600.

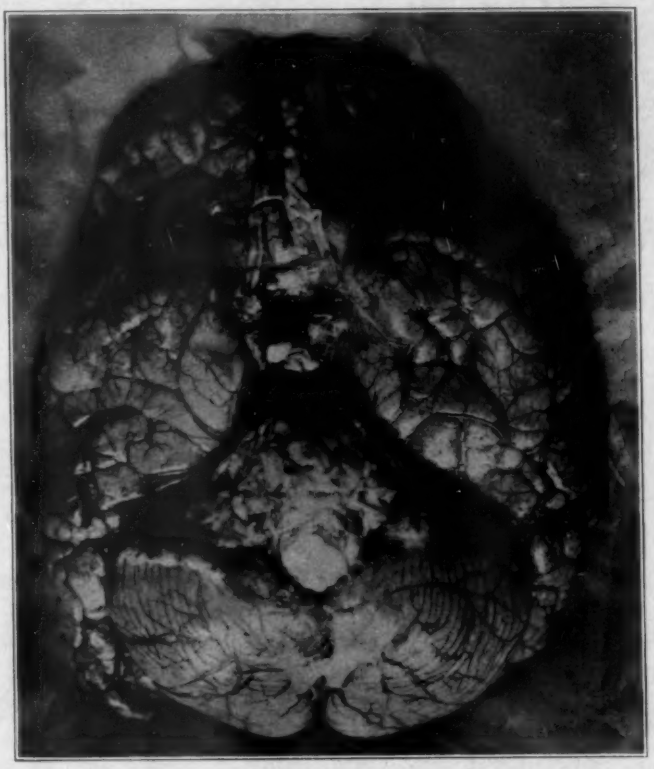

Fig. 2 (case 3).—Ringlike exudate in bulbar meningitis beginning in the pontile cisterna and extending around the hair stem.

October 11: The patient was restless but there was no headache or other sign of meningeal irritation.

October 13.—The temperature again reached 105 F., following a chill. There was no headache. The patient was slightly irrational and pulled the tube from his throat.

Within a few hours he presented the typical picture of bulbar cisterna meningitis. He lay on his back with the eyes closed, but could be aroused; there was a slight stiff neck, but no more than was present ever since injury. There was incontinence associated with a high temperature, slight restlessness, but no headache. Lumbar puncture revealed milky fluid not under pressure; the cell

count was 2,800; the globulin reaction was 3 plus, and micro-organisms were found, probably streptococci.

The patient died twenty-four hours later.

Postmortem Examination (Dr. Harrison S. Martland).—Postmortem examination revealed fracture of the anterior portion of the body of the third cervical vertebra, surrounding which was a sloughing infiltrated mass, a dissecting abscess between the bone and mucous membrane, with many thrombosed vessels. The fracture did not enter the spinal canal. The bone of the base of the skull was normal.

Meninges: Purulent exudate filled the bulbar cisterna on the anterior surface of the pons, from which it extended under the inferior surface of the cerebellum, and followed the basilar artery upward into the region of the third nerve and into the chiasmal cisterna from which a little exudate ascended into the sylvian fissure. There was no exudate on the superior surface of the cerebellum. Opening of the venous sinuses disclosed a purulent clot on the region of the torcular Herophili.

The internal organs showed signs of general sepsis.

Postmortem Comment.—The pus over the inferior surface of the cerebellum was apparently an overflow, the same as the slight amount of pus in the sylvian fissure. The infection must have entered the meninges through the pterygoid or pharyngeal plexus of veins.

The pus in the region of the torcular may have been secondary to the meningitis or simply a part of the general venous sepsis.

CONCLUSIONS

The abducens is the most primitive of the ocular motor nerves and is in intimate relationship with the mesoblastic tissues of the cranial base, consequently it is most frequently paralyzed by suppurative lesions; not, as is generally supposed, because of its long course. These intimate relationships do not vary greatly in different cadavers and on the two sides of the same cadaver.

Abducens paralysis of the homolateral or contralateral side, when associated with a suppurative lesion, should be considered as only a small part of the clinical picture in the localizing of the site of the lesion or the nature of the process.

The periosteo-aponeurotic dural nature of Dorello's canal and the peri-dura-arachnoid structure of the fifth nerve furnish a satisfactory anatomic explanation of the different clinical types of fifth nerve irritation and abductor paralysis in those cases in which recovery follows after mastoid exenteration. The evolutionary development of the first branch of the trifacial and its anatomic connectives furnishes a satisfactory explanation of the significant "pain behind the eye" in caries of the petrous apex.

In the differential diagnosis of the types of meningitis, a proper appreciation of (*a*) the various causes and forms of facial pain and (*b*) abductor paralysis and the recognition of the (*c*) syndrome of bulbar cisterna involvement must play an important part.

Both facial pain and abductor paralysis in suppurative diseases of the middle ear furnish valuable localizing information for the diagnosis between intradural and intra-arachnoid inflammation, if the surgeon distinguishes between congestion and caries—and between intra-Dorello and intracranial involvement—as he diagnoses facial paralysis of central and peripheral origin.

Properly interpreted, either facial pain or abductor paralysis will enable a localizing diagnosis of (*a*) caries of the apex of the petrous pyramid, (*b*) localized pontile cisterna meningitis as the result of such caries, (*c*) suppuration of the sphenoidal sinus, and (*d*) thrombophlebitis of the cavernous sinus and associated petrosal and basilar veins, all at a time when surgical intervention promises hope for recovery.

In the benign cases, temporofacial pain is a referred pain from irritation of a sensory communication from congestion of the bone in that portion of the anterior surface of the petrous pyramid where the geniculate ganglion, superficial great petrosal and vidian branches of the glossopharyngeal nerve are given off, as in this region the nerves are in bony canals, are extradural, and cannot be separated from the bone. The osseous congestion or dural irritation originating the pain may be more or less quiescent, and still cause pain for a considerable period.[19]

Thus temporofacial pain, or even a neuralgic pain in the supra-orbital region around the eye, or in the face or teeth, associated with or following an otitis, if unaccompanied by signs of sepsis, cerebral irritation or labyrinthitis, simply calls for a complete removal of the mastoid cells with their perilabyrinthine cellular connections. This having been done, the continuation of the pain only becomes of serious moment whenever the sepsis continues.

First branch pain—pain behind the eye—in the presence of sepsis is significant of caries of the petrous apex from dural pulling of the middle fossa; and if unrevealed by mastoid examination, or if associated with signs of posterior fossa irritation—bulbar meningitis, irregular stiff neck, sixth nerve paralysis—it calls for the opening of the apex.

Symptoms of localized pontile meningitis originate from irritation of the cortex of the anterior surface of the pons, and when it follows caries of the petrous apex, the meningeal signs of cortical bulbar irritation follow symptoms of osseous and dural disease of the middle fossa.

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19. Forks, S. B.: Gradenigo's Syndrome, Arch. Otolaryng. **7**:363 (April) 1928. (Had temporoparietal pain with loss of sensation in the face and external rectus paralysis, two years after the ear had ceased discharging and the drum healed.)

Data on Anatomy of the Sixth Nerve as Presented by Dissections on Nine Cadavers (Seven Fresh and Two Dry)

Dural Portion	First Cadaver	Second Cadaver	Third Cadaver	Fourth Cadaver	Fifth Cadaver	Sixth Cadaver	Seventh Cadaver	Dry Cadavers 00 and 0
Is it adherent to periosteum?	Dura is part of and contiguous to periosteum; can only be separated by tearing	.....	Left nerve, yes; by fibrous tissue; part of the periosteum; forms the sheath of the nerve	Periosteum forms a sheath to the nerve on three sides	No	Nerve makes rather a sharp bend over the bone and while it can be separated from the bone, there are many adhesions going to the bone	Yes; right gasserian ganglion slightly adherent to the bone	No, but any inflammation of the periosteum of the apex of the petrous tip would raise the sixth nerve against the occipitocondyloid ligament
Is it compressed by canal or not?	No	No	Yes	Could not be easily compressed by elevation of the pons	No	No	Right: One branch is in small canal and cannot move freely Left: Not so much	Canal so completely surrounds the nerve that it has to be elevated to be seen
Is nerve held to floor?	No	No	Yes	Yes	Left: Yes Right: No	While it can be separated from the bone there are many adhesions from the nerve going to the bone as it ascends over the tip it is these fibers from the ligament that hold the nerve down	Right: Internal branch attached to dura Left: Also attached but looser	
Can the nerve be elevated?	Yes	Yes	No	With difficulty; elevation gives the impression that it might easily be compressed against the sharp upper lip of the canal	.....	Moves freely in canal	Right: Outer branch; moves freely in canal	In Dorello's canal
Does it travel in dural layers?	Yes	Yes; apparently a dural covering which surrounded the whole nerve in its course, 3 mm., until it passed free into the cavernous sinus	It is covered by the pia-arachnoid on the anterior surface of the pons, and as it leaves the pons it carries a reflection of arachnoid	.....	.....	.....	Right: Internal branch; cannot move freely in canal, but the two branches continue separate into the cavernous sinus	
Is it on petro-occipital articulation?	Directly at suture	.....	Right nerve is well external to the articulation; the bone is on the outer surface for a long distance there being a distinct groove running upward, forward and inward	.....	Yes	Nerve is in the ligament coming from the articulation, not in the bone at all; it is the fibers from this that hold the nerve down; articulation of petrous from occipital easily separated	Left: Internal to articulation	OO: Right suture widely open, left closed; line of articulation dim O: Inside suture uniting petrous pyramid to the occipital
Is the nerve external on petrous bone?	.....	Yes	Yes	Yes; entire length, 3 mm., to where it turns forward		Yes	Right: Inner branch is on the bone; outer branch on ligamentous fibers of the articulation of occipital and petrous	Rises in canal 0.5 cm. passing under the stylo petrous ligament below the posterior clinoid process at the posterior border
Is the nerve on the articulation of the occipital?	Yes	Yes	.....	.....	Yes	Directly over suture	Right: Outer branch or ligamental fibers of the articulation of occipital and petrous Left: On articulate fibers in dura, but after passing edge is on bone	

Bony Portion								
Is tip areolar?	.....	.....	Yes	.....	Nerve held down by fibrous tissue forming the periosteum, tip and bone under the nerve areolar, some areolar tissue connects the superior semicircular canal with the middle ear	.....	.....	.....
Connection of bone cells with those of middle ear	Area is behind carotid canal; communicates through cells; is contiguous to posterior inner arm of the opposite sphenoid sinus which here bends inward behind the small sphenoid of the same side	Large cells in the tip which runs inward and forward into the carotid canal region; cellular tissue of the tip extends downward under the gasserian ganglion which is slightly adherent to the bone of the gasserian fossa	Large pneumatic cell directly under the nerve communicates outward to the semicircular canal by spongy bone with a small opening of the canal at the basal cisterna		Cells of the petrous reach backward along the superior border to the superior semicircular canal then go down and forward to the region of eustachian tube	.....	.....	Left: Cell behind petrous tip in gasserian ganglion communicates by cellular tissue which ends at superior semicircular canal; they are continued forward in front of carotid canal; cells under labyrinth are well marked but macroscopically do not reach the region of the middle ear Right: Bone under sixth cellular; it does not reach the semicircular canal
Relation of Petrous Cells to Fifth Nerve	Has communication with the carotid canal through cells and is contiguous to the posterior and inner arm of the opposite sphenoid; cellular tissue of the tip extends downward under the gasserian ganglion; inflammation of lining cells of tip would probably irritate the fifth nerve	The whole region is so cellular that inflammation of the lining cells of the tip would probably cause irritation of the fifth nerve	.....		On right side, intra-arachnoid portion is very long, the canal being situated much nearer the inner border of the fifth nerve than usual; no cells are seen in the superior border of the petrous, but a great deal of fibrous tissue; on the petrous tip itself there are cells and also many soft cells inside on the occipital; the sinus disappears but probably turns inward to form mesh on the bulbar side of the sphenoid process; suture of articulation goes from posterior to anterior surface	Right: The nerve is attached to the internal branch of Gruber's ligament, which here divides; this branch becomes part of the dura; removing the bone it is cellular		
Distance Below Inner Margin of Fifth Nerve	.....	....	.....		Opening is about 7 mm. on both sides; for the sixth nerve it is 0.25 cm. below the opening for the fifth; on both sides the openings are high and medially situated	8 mm.	7 mm.	1 cm. below inner border of foramen for exit of fifth nerve

Data on Anatomy of the Sixth Nerve as Presented by Dissections on Nine Cadavers (Seven Fresh and Two Dry)—Continued

Bony Portion	First Cadaver	Second Cadaver	Third Cadaver	Fourth Cadaver	Fifth Cadaver	Sixth Cadaver	Seventh Cadaver	Dry Cadavers 00 and 0
Internal to the articulation of the occipital?	.....	.....	.....	.....	.....	Passes to outer part of canal under bony part of petrous	.....	00: Line of articulation hardly visible 0: Internal to suture uniting the petrous pyramid to the occipital
In Passage from Posterior into Middle Fossa								
On which bone does it pass forward?	At the petro-occipital suture	At the crest where it passes from the posterior to the anterior surface on fibrous tissue, which unites the petrous pyramid with the sphenoid 12 cm. lateral to the ascending wall of the posterior clinoid process	.....	.....	Petro-occipital	Passes to outer part of canal under bony part of petrous, only half of nerve being under ligament at all	Left: Crosses occipital Right: Inner branch is on occipital and petrous; outer branch ligamentous fibers	Inside the petrous
Does nerve pass under tip of petrous or not?	Yes	Yes	.....	Yes; same condition on the left side where passing is still more visible	.....	Passes to outer part of canal under bony part of petrous; removal of bony sphere above shows nerve making rather sharp bend over bone	.....	Beyond Dorello's canal; goes forward in cavernous sinus below postclinoid process
Does nerve turn at acute or obtuse angle?	Nerve turns at a right angle under the ligament	Turns to a right angle under Gruber's ligament	.....	.....	.....	Makes sharp bend over bone	Left: Bends under Gruber's ligament in dura, but neither left nor right makes sharp turn	
Direction of Gruber's ligament	Hardly marked; on removing the outer dural layers the nerve passes under the ligament and turns nearly to a right angle	Hardly marked; on removing the outer dural layers the nerve passes under the ligament and turn nearly to a right angle; movable	Nerve runs upward and slightly outward under a well developed petro-sphenoid ligament which runs markedly upward as well as forward and inward; this is dissecting the right canal; the canal under the ligament is very smooth	Nerve immediately enters a large cavity, the ligament being 0.5 cm. away; canal under ligament in the area of the pyramid, 0.5 cm. long	Left Side: Runs upward and inward; well developed, considerable room under ligament Right Side: Nerve passes under the ligament; appears to divide into two parts at outer attachment; the nerve is attached to the internal branch; this becomes a part of dura; bone cellular	Well developed direction in and forward with upward direction of about 15 degrees; good-sized cavity below ligament; nerve is on the ligament coming from the articulation; ligament 5 mm. long	Right: Gruber's ligament not seen Left: 8 mm. in length in dura	Ligament well seen; runs vertically upward and inward; sixth nerve passes to outer border with the bone only covered by the periosteum
Character of Bone Compact or cancellous?	Cancellous; one cell of good size broken into with layer of cancellous tissue surrounding it	Cancellous	Spongy bone directly under the right nerve	Fibrous tissue fills the suture between the petrous tip and the sphenoid process of the occipital (see general remarks)	Cancellous	.....	Left: Bone under nerve spongy; petrous tip was large cell directly behind gasserian ganglion	

Bulbar Portion								
Direction in bulbar cisterna	Upward in the direction of the posterior clinoid process	Upward in direction of the posterior clinoid process	Directly upward so that it lies on the surface of the pons like a network	Upward and inward; right canal slightly lower than the left; direction of the left, inward and slightly upward	Left: upward and inward; right, directly upward	Foramen 45 degrees to the midline; oval opening, inward, forward and upward	Left: Canal runs upward; Right: Inner opening straight up	
Length of nerve in bulbar cisterna	.....	.....	From leaving the bulb to entrance into the dura, 2 cm	.....	.....	.....	.....	
Size of nerve	Right side: Nerve rather large	Right side: Nerve rather large	Right nerve, large; left, larger	.....	.....	.....	Right: Double; both branches long and frail; in cavernous sinus one branch three times larger than the other Left: Rather frail; about size of right; outer and larger upward and slightly inward	
Distance between openings into Dorello's canal, left and right	.....	.....	2 cm.	2.2 cm.	2 cm.	2.5 cm.; left on a higher plane than right	Left: 1 mm. lower than right; Left to right (internal branch) 1.5 cm.; (external) 1.7 cm.	Gives impression of no canal; long diameter almost vertical on left side, opening upward and inward; right side is the same but 3 mm. lower, diameter 5 or 10 degrees toward sagittal suture; distance between second and sixth nerve, 1.6 cm.
Size of opening into Dorello's canal and direction of nerve	Upward in the bone	.....	Right foramen higher than the left; direction upward and inward; left, almost inward and smaller than the right	Right: upward and inward less than 45 degrees from horizontal	Right: opening forms an oval slit directly upward	Oval opening; inward, forward and upward	Left: Upward Right: Upward and slightly inward	Nerve enters canal a long way down; canal goes almost directly upward but axis is vertical
Dorello's Canal Portion	.....	.....	.....	.....	.....	.....	.....	
Length of nerve in Dorello's canal	.....	3 mm. in the dura, until it passes free into the cavernous sinus	.....	Dural course, 1 mm.	Runs up to 3 mm. before reaching ligament	4.5 mm. in canal before turn	Left nerve long in dura, 8 mm.	OO: Not plain O: Long, right 2 mm. longer than left, rises in canal 0.5 cm.
On bone or fascia	On bone	.....	Right nerve is on the bone itself	On bone	Left nerve held down to the bone by fascia and runs over the fascia at the articulation; the bone can be separated at the articulation	.....	Left: In its dural course it was on the articulate fibers, but as it passed over the edge is on the bone; in its dural course is held down by dural fascia	

Data on Anatomy of the Sixth Nerve as Presented by Dissections on Nine Cadavers (Seven Fresh and Two Dry)—Continued

Bulbar Portion	First Cadaver	Second Cadaver	Third Cadaver	Fourth Cadaver	Fifth Cadaver	Sixth Cadaver	Seventh Cadaver	00 Cadaver 0 Cadaver
General Comments	Any inflammation of the tip cells of the petrous or sphenoid of the opposite side, or of the carotid canal might give paralysis of the sixth nerve by swelling of the periosteum in the canal of the dura before the ligament is reached, the direction of the nerve being upward in the bone In the first, second and third cadavers the dye goes in the collar between the brain stem and cerebellum on its superior surface (inner third), and in the fold of the cerebellum behind and above the pons the pigment is in the arachnoid prolongation of the vessels running from the third nerve backwards, and spreading out over the superior collar and lateral pontile cerebellar angle	Could not be affected from the sphenoidal sinus by reason of its outward position; sphenopetrosal ligament also could not compress it	In this cadaver the sixth nerve runs directly upward from the exit in the brain between the pons and medulla at a point opposite to an eminence below the jugular foramen, which passes forward and slightly upward across to the opposite side; it does not go quite to the top of the pons, which seems to reach the margin of the posterior fossa's tentorial reflection forward in the region of the third nerve The periosteum of the bone forms the sheath of the nerve and any inflammation would compress the nerve; in this pneumatic and spongy petrous bone, the small opening of the canal, the large nerve held down to the bone by the periosteum covering the pneumatic and areolar spongy bone are factors in paralysis. Dye goes across above the bulbar cisterna by way of the third nerve region, descends on the upper collar, practically no pigment being on the pons	Sphenoidal process of the occipital bone of ivory hardness; after getting through it on the border encountered cells covered by compact bone of 2 mm. thickness. In this is deep fissure through which runs inferior petrosal sinus below the region of the superior border. Liability to sixth nerve paralysis from swelling of periosteum would be very little, but an inflammation of the middle ear could be carried through the cells to the apex and cause compression of the nerve from above and below, although the ligament would have nothing to do with it	An inflammation of the dura would cause pressure by extending to Gruber's ligament which had a direction almost directly downward	Inflammation of the fibers of the articulation of the two bones might cause pressure and inflammation because of its adhesion to the aponeuroses; articulation of the petrous from the occipital easily separated; no ossification Surgical lesson: The pontile cisterna protects itself from infection because, although it is large, the basilar artery is firmly held down to the brain and the cisternal space does not open freely; the inner pial membrane not being held apart as in the chiasmal cisterna; normally, they are aproximated and thus adhesions from inflammation would easily occur; fluid holds them apart; if they could be aspirated the adhesions would immediately seal off the area and the exudate become organized; the bulbar cistern is not a wide open space but united by bands from the arteries in the median line; the surgical opening of the internal auditory prolongation drains the angle externally; by opening the fifth arachnoid prolongation the bulbar cisterna is reached higher and more mesially	Inflammation of the dura would compress the right nerve as it travels in dural layers, and cannot move freely in dural canal	Entrance of the sixth nerve into the dura is in the crotch opposite the cerebellopontile peduncles; any swelling of the cerebellum or exudate in the bulbar cistern might cause compression; certainly pontile tumors and abscesses of the cerebellum will give a bilateral paralysis to the sixth nerve before it enters the canal

Consequently, the symptoms of localized bulbar meningitis of otitic origin can be summarized as (1) a period with signs of dural irritation of the middle fossa, of which facial pain, especially pain behind the eye, is the most significant (possibly associated with abductor paralysis), followed by (2) symptoms of arachnoid inflammation of the posterior fossa near the median line. Localizing middle and posterior fossa symptoms are thus (3) in combination one with the other; (4) semicoma from which the patient can easily be aroused, (5) supine position, on back, with eyes closed, (6) intermittent recurrence of vertical nystagmus. All these are signs of posterior fossa involvement, but without severe headache, great restlessness and opisthotonos of cortical meningitis, although accompanied by high fever and rapid pulse.

(7) Repeated trials of visual fields may reveal great bilateral variations and the sudden appearance of a bitemporal hemianopsia somewhat resembling pituitary tumor pressure.

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THE NATURE OF EWING'S TUMOR*

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INTRODUCTION

From among the reports of cases of malignant tumors of the bone in the Surgical Pathological Laboratory of the Johns Hopkins Hospital representing in all a total of more than 400 cases, a series of 60 cases which were grouped under the name of periosteal round cell sarcoma or Ewing's endothelial myeloma were selected for the present analysis.

The result of this analysis has brought forth many interesting and novel features in the natural history and clinical course of this tumor,[1] Under the direction of Dr. Bloodgood the cases were first studied microscopically and later correlated with clinical data, the prognosis and ultimate result being made available in fifty-two of these cases by clinical follow-ups.

Ewing's sarcoma is essentially a disease of early life, the majority of the tumors occurring during the first two decades (95 per cent). The age incidence ranges between 4½ and 44 years. The males affected predominate over the females in an approximate ratio of 2:1, and only one negro was affected in the series.

The bones most frequently involved were those of the long pipe bone class, although the ilium, scapula, clavicle, skull and bones of the feet were affected in a few instances. In no case was the primary location of the tumor on other than the shaft side of the bone. An almost equal number of cases were found divided between the right and the left sides of the body. Those bones most readily subjected to trauma were found to be the most frequently affected, that is, the femur, tibia, humerus, fibula and pelvis, the tibia leading the list with involvement in fifteen cases.

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1. Copeland, M. M., and Geschickter, C. F.: Ewing's Sarcoma, Arch. Surg. **20**:246 (Feb.) 1930.

SYMPTOMS

Trauma was recorded in twenty-two cases and in every instance was definitely related to the subsequent onset of clinical symptoms. The average latent period noted between the time of trauma and the clinical onset of symptoms was approximately five and one-half months.

Pain was an outstanding symptom in fifty cases (83 per cent) and was noted as the first symptom in twenty-one cases (35 per cent). It usually began spontaneously, though in some cases it followed trauma and tenderness by a more or less short period, often appearing simultaneously with tumor formation. Most frequently the pain was first intermittent, lasting from a few hours to several days, subsiding at intervals but recurring each time in a more severe form. The intervals between the attacks appeared to become shorter in duration, until a constancy of pain was noted by the patient. Nocturnal pain was found to be the most severe in many cases.

In fifty-six cases (90 per cent) a mass could be palpated, and in 19 per cent of the cases it was complained of by the patient as the initial symptom. The average duration of tumor formation, as noted by the patient before coming under observation, was thirteen and one-half months. The tumor masses varied from small localized swellings to large fusiform masses, extending along almost the entire length of the affected bone. Peripheral disturbances about the tumor were manifest in the form of vasomotor changes, often giving the skin a somewhat more red or bluish tint than that of the surrounding cutaneous areas. The soft parts, though usually freely movable were often edematous. In many instances recorded, local elevation of temperature was found over the tumor mass. On palpation the tumors usually presented a hard indurated swelling, apparently continuous with the sheath of the bone. Fluctuation of the tumor was not noted, though there were varying degrees of resilience, all the growths being less hard than bone.

In some of the tumors there was a tendency to decrease spontaneously in size, with sudden cessation of pain. The variability in the size of the tumor is to be associated with hemorrhage and its absorption.

Pathologic fracture was of relatively rare occurrence, being noted in only three cases (5 per cent) in the series. Two fractures were in the upper shaft of the femur and one in the lower shaft.

As was pointed out in a previous communication, among the malignant tumors of the bone, the greater number of pathologic fractures (62 per cent) are found in association with multiple myeloma, while other types similarly affected by fracture are, in the order of their frequency: bone cysts, 45 per cent; giant cell tumor, 14 per cent, and

osteogenic sarcoma of the bone, 8 per cent.[2] Thus, among the types of tumor of the bone complicated by pathologic fracture, Ewing's sarcoma presents the minimum number of cases.

The constitutional reaction of the body to tumor invasion reveals a variable response in different patients.

The range of temperature elevation is between 99 and 104 F., the average being 100. These elevations in temperature were commonly observed late in the disease after metastases had occurred, but fever was also noted early in the clinical course in 30 per cent of the cases. A slight albuminuria together with a few white and red blood cells in the urine was often associated with the fever. Though Bence-Jones bodies were not sought as a routine procedure in this series of cases, these bodies were not found in a single instance when the test was carried out.[3]

In thirty-one cases in which complete blood counts were made, the blood picture ranged from that of the normal type to that of a secondary anemia and from a relative leukopenia to a considerable leukocytosis. The white blood count and its differential count presented no unusual peculiarities. Twenty cases showed more than 10,000 leukocytes and three had a count of 20,000, the average in these cases being 15,200 white blood cells; this is often a source of confusion leading to the diagnosis of osteomyelitis. The differential count, except for an occasional eosinophilia ranging from 4 to 20 per cent, was within normal limits.

The patients showed great variability in nutrition. In some cases a noticeable loss of weight was observed early in the course of the disease over a relatively short period, while in other cases there was little or no evidence of undernutrition until near the termination of life. The terminal phases of the disease revealed a progressive emaciation in most of the patients observed.

Internal metastases usually present themselves clinically late in the disease.

As seen by the x-ray, Ewing's sarcoma is most often diffuse and is situated near the midshaft of a long bone. The earlier lesion presents the more difficult diagnosis, and in this disease the difficulty is enhanced by the variability in the appearance of the bones affected and infiltrated by the tumor. The neoplasm expands the shaft of long bones by a diffuse infiltration of the region, which results in widening and increased density of the cortex and a mottling of the marrow cavity, due to areas of increased density. Both new bone formation and bone destruction are secondary to infiltration of bone by the tumor

2. Geschickter, C. F., and Copeland, M. M.: Multiple Myeloma, Arch. Surg. **16**:807 (April) 1928.

3. Boggs and Gutherie: Am. J. M. Sc. **144**:803, 1912.

(fig. 1). In the early case, bone formation predominates, giving rise eventually to either parallel or radiating spicules of new reactive bone. In the later stages of the disease, bone destruction, both medullary and cortical, characterizes the x-ray picture.

The roentgen studies presented here do not support the view that Ewing's tumor is a lesion that is primarily destructive of bone;[4] in six of seven early cases the first evidence of tumor infiltration was an

Fig. 1.—A roentgenogram showing bone formation and bone destruction. The periosteal reaction with parallel layers of reactive bone, characteristic of early Ewing's sarcoma, should be noted.

increased density of the bone. The typical contour of the involved area in the bone is also against the current conception of the medullary origin of this neoplasm. On a physical basis, one would expect medullary tumors to show an approximate spherical shape in the roentgeno-

4. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928.

gram, because their expansion is unhindered in three and usually in four directions. In contrast to this, the area infiltrated by Ewing's tumor is generally elliptic, with its long axis parallel to the shaft of the bone, indicating that the growth is resisted in the two opposite directions.

PATHOLOGIC CHANGES

An analysis of the gross pathologic changes aids materially in the interpretation of the roentgen observations. The tumor is usually

Fig. 2.—A gross specimen in longitudinal section showing the primary involvement of the shaft with secondary invasion of the epiphysis. It should be observed that the bulk of the tumor is beneath the periosteum and outside the cortical region.

located on the metaphyseal side of the bone, the epiphysis being secondarily involved in only three instances. Regardless of the site of origin of the tumor, all the gross specimens with one exception showed the bulk of the tumor lying subperiosteally (fig. 2). The medullary cavity in some instances contained a small portion of the tumor, but usually this region was constricted or totally occluded by new reactive bone (fig. 3). The widened cortex as pictured in the roentgenograms

is shown in the gross specimens to be made up of subperiosteal and endosteal new bone formation, which encroaches on the medullary space and frequently seals it off from tumor invasion. The tumor appears to infiltrate rather than to destroy bone in its early stages, and the bone thus infiltrated reacts vigorously with new bone formation, but this bone may subsequently undergo destruction when surrounded and infiltrated by tumor, apparently because of the interruption of the blood

Fig. 3.—A gross specimen in longitudinal section showing endosteal reaction, which is sealing off the medullary cavity by reactive bone in an attempt to overcome tumor invasion.

supply where the tumor has invaded and blocked both the Volkmann's and the haversian canals (fig. 4).

When the involvement of the bone by the tumor is diffuse, the subperiosteal reaction of new bone formation is both parallel and at right angles to the cortex. The origin of this bone is explained by the

mode of advance of the tumor through the haversian system and Volkmann's canals. The parallel deposits of new bone appear to be the result of bone proliferation from the subperiosteum and peripheral layers of the cortex, when the periosteum has suffered minute separation from the cortex, giving an onion peel-like formation characteristic of the early roentgenographic appearance (fig. 1). With increased separation of the periosteum, spicules of new bone arising either from the cortical region or from beneath the periosteum are laid down at

Fig. 4.—A gross specimen taken late in the disease, showing the ultimate destruction of the cortical bone, apparently due to interruption of the blood supply where the tumor has invaded and blocked both Volkmann's and the haversian canals.

right angles to the shaft rather than parallel (fig. 5). We [5] agree with Ribbert that this fact is due to the vessels perforating Volkmann's canals, which determine the direction of the new growth of bone when

5. Buerger, L.: Further Studies of Sarcoma of Bone, Am. J. M. Sc. **140**:355, 1910.

they are pulled outward in maintaining their continuity with the periosteum, after it has been elevated. This determination of bone pattern by vessel units is typical of the embryo and is not lost in the adult. The soft part tumor is usually encapsulated by a thin layer of fibrous tissue, which at the margin of the growth is seen to be continuous with the periosteum. The tumor tissue itself is a firm but granular, grayish-white substance divided into characteristic lobules by

Fig. 5.—Roentgenogram of Ewing's sarcoma showing osteophytes at right angles to the cortex, together with a thickening of the cortical bone. It should be noted that this reaction is diaphyseal in location.

a number of connective tissue strands, extending from the outer capsule to the region of cortical bone. Occasionally, cysts are noted in the tumor substance.

The microscopic pathology is one of the most uniform characteristics of the disease, revealing a more or less constant cellular morphology. The type of cell in compact areas is small and polyhedral, with a

round or oval nucleus (fig. 6). The cytoplasm is quite scanty and practically stainless. The nucleus is deeply stained, showing a definite limiting membrane with a sparse number of chromatin granules scattered through the nucleus without definite arrangement. Nucleoli are rarely seen, but mitotic figures are frequently noted. Little pleomorphism is observed, and multinucleated cells of tumor origin have not been noted, this being an important matter in the microscopic diagnosis.

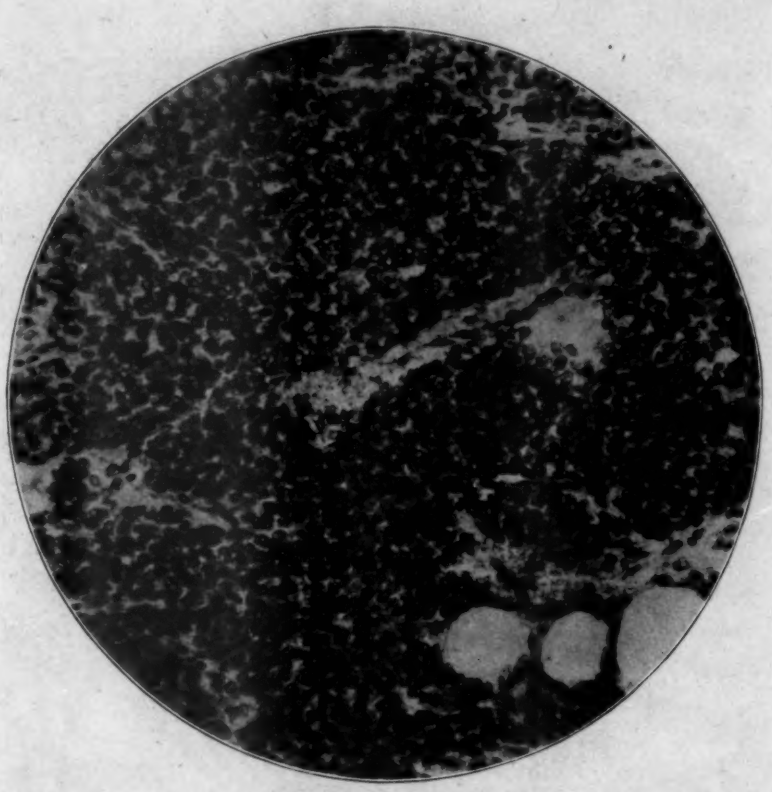

Fig. 6.—Photomicrograph showing the uniformity in the size of the cells and the indistinct cytoplasm with round and oval nuclei.

There appears to be no intercellular stroma in the tumor (fig. 7), but fibrous trabeculation divides the neoplasm into lobules, where it is found subperiosteally. These septums often give the tumor an alveolar arrangement.

Vascularity is variable in these tumors and may be pronounced. In some sections taken through areas of bone, haversian canals occupied by blood vessels were infiltrated by the tumor, the tumor cells sometimes lying within and sometimes without the vessel walls (fig. 8).

Phenomena of this character have been cited by some authors as evidence of the seat of origin of the tumor, but we are inclined to the belief that in most of these instances tumor cells are following the path of least resistance in their invasion of bone, traversing the haversian systems.

Areas of fibro-ostosis[6] (osteitis fibrosa), either subperiosteal or endosteal in origin, are seen where the tumor is invading bone, and constitute a healing reaction (fig. 9).

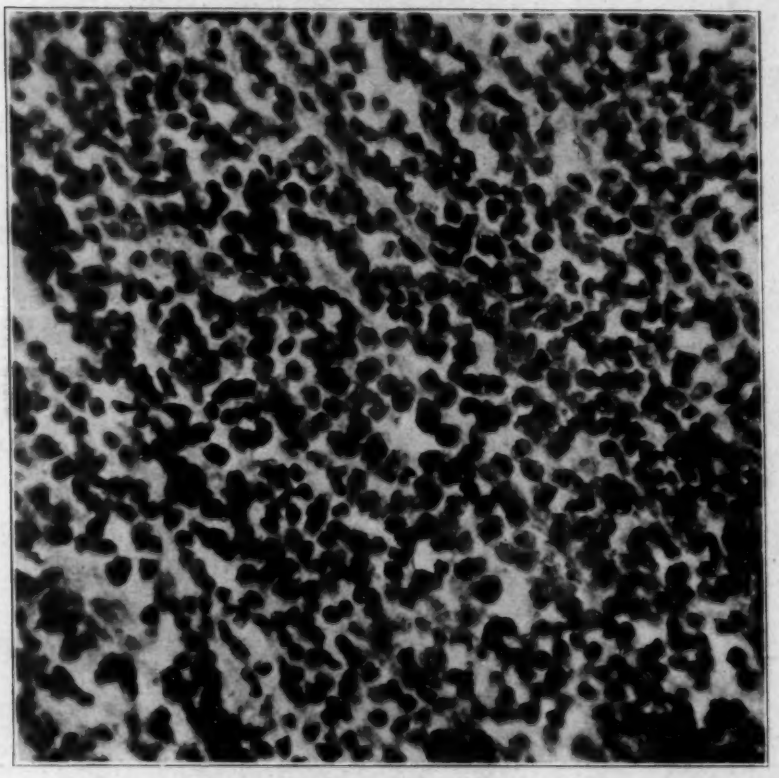

Fig. 7.—Photomicrograph of Ewing's sarcoma. Observe the lack of intercellular stroma.

Necrotic areas of tumor are often noted surrounding islands of tumor cells through the center of which a blood vessel passes, the blood supply apparently being inadequate for more than the tumor cells immediately surrounding the vessel. The periphery of these tumors is frequently infiltrated by cells of the polymorphonuclear or monocytic types. This round cell infiltration is most common in the tumors of

6. Geschickter, C. F., and Copeland, M. M.: Osteitis Fibrosa and Giant Cell Tumor, Arch. Surg. **19**:169 (Aug.) 1929.

longer duration or in those which have previously been explored, and not infrequently leads to an erroneous diagnosis of osteomyelitis at biopsy. Plasma-like cell infiltration was noted in a few cases, and this possibly may have no special relation to the tumor, as sections of normal bone sometimes show such cells. On the basis of finding these cells, certain authors have suggested a relation between this tumor and multiple myeloma.[7]

Fig. 8.—Photomicrograph showing a portion of the cortex of a bone. The haversian canals have been widened by the infiltration of tumor which has pervaded the bone by means of the perivascular lymphatics within the haversian canals.

Dissemination and metastases have occurred in every case of the series which so far has terminated fatally. The extent of metastases

7. Ewing (footnote 4). Kolodny, A.: Bone Sarcoma, Surg. Gynec. Obst. **44**:126, 1927.

has been most difficult to localize because of the insufficient data included in many of the case reports, while necropsy has been performed relatively rarely in the series. Only those fatal cases in which there has been definite proof of metastases have been reported in this discussion, although every patient is said to have died of tumor. The most frequent sites of metastases are the lungs, the lymph glands and the skull.[3] The most unique feature in the dissemination of Ewing's tumor

Fig. 9.—Photomicrograph showing osteitis fibrosa surrounding the area of tumor invasion. Observe the osteoid spicules surrounded by osteoblasts and fibrous tissue. See figure 1.

is the predilection of the secondary growths for other bones. Though some observers view this dissemination to other bones as a proof of the fact that the tumor is primarily a multiple disease of the skeleton, in our series it was nearly always possible to obtain a definite latent period of from two and a half months to a year between the appearance of the tumor in the single initial bone and the secondary involvement of other bones.

The bones most frequently involved by metastases are the skull, spine, scapula and clavicle, although dissemination may occur in the long pipe bones.

Though the involvement of the single bone early in the disease with later dissemination of the neoplasm to other bones constitutes a unique and important feature of the disease, it is unusual for the patient to present himself for examination with more than one bone involved, and a single focus usually predominates in size as well as in the duration of its growth.

In reviewing the many diagnoses first made and later revised in cases of Ewing's tumor, it is interesting to note that inflammatory diseases of the bone predominate. A primary diagnosis of pyogenic periostitis or osteomyelitis was made in ten cases, tuberculous disease of the bone in nine cases, syphilitic periostitis or osteomyelitis in six cases and typhoid osteomyelitis in one case, thus showing the frequency with which Ewing's tumor is confused with chronic inflammation of the bone. Clinically, multiple myeloma was noted as a source of confusion in two cases, and literature on Ewing's sarcoma involves osteogenic sarcoma and metastatic carcinoma as sources of confusion. Since space here does not permit going into a differential diagnosis of Ewing's sarcoma, suffice it to say that biopsy is most often resorted to in making the diagnosis (fig. 10).

At the present time we have complete follow-up reports in fifty-two cases of Ewing's sarcoma. Forty-three of the patients are dead and eight (13 per cent) are living and apparently well, with an average duration of life of seven years and eight months following the initial symptoms.

TREATMENT

We have divided the methods of treatment into three main groups for analysis: (1) amputation or resection with irradiation; (2) amputation or resection without irradiation, and (3) irradiation alone or with exploratory operation.

In group 1 are thirteen patients in whom the postoperative duration of life averaged 29.2 months; three (22 per cent) of this group are well, with an average duration of life extending over a period of five years and seven months.

In group 2 are twenty-four patients with an average duration of life extending over a period of twenty months; four (16.5 per cent) of this group are well, the average duration of life extending over a period of six years.

In group 3 are eight patients with an average duration of life of twenty-seven months. One patient of this group is living after fifty-three months, curettage having been performed prior to irradiation.

Coley's toxins apparently have had no effect on the duration of life, whether the toxins were given alone or were combined with other forms of treatment.

The weight of evidence at this time seems to indicate that the patient should receive the benefit of both radical operation and roentgen treatments when the tumor is observed in the usual location prior to the formation of metastases.[8] Exploration does not necessarily affect

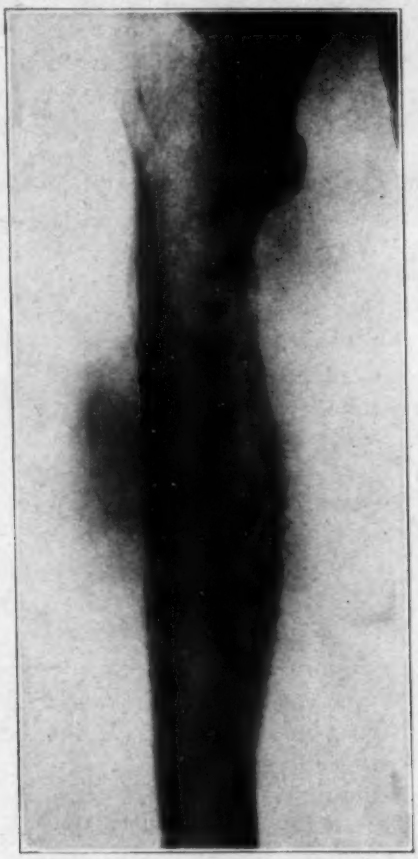

Fig. 10.—A roentgenogram of Ewing's sarcoma in the femur which is not unlike early inflammatory disease of the bone.

the prognosis of the disease when radical operation or roentgen treatment follows this procedure. In two patients living after five years, exploration was done before the operation of choice was resorted to. In six cases in which exploratory operation without further treatment

8. Bloodgood, J. C.: Bone Sarcoma: Periosteal and Diffuse Type and their Diagnosis from Benign Lesions, J. Bone & Joint Surg. **8**:727, 1926.

was performed, death occurred in from one to twenty-two months. One patient who received Coley's toxins alone died fourteen months after the therapeutic procedure was begun.

COMMENT

When the facts brought out by the analysis of this series of cases are listed, they point to the conclusion that the tumor is a malignant sarcoma of the bone. In favor of this is the age incidence of the tumor, its location in bone, the cellular nature of the pathologic changes, the metastases and the high percentage of fatality. Against the opinion that this lesion is a metastatic tumor arising primarily outside of bone is the failure to demonstrate such a primary focus in any of the cases studied; the cellular morphology of this tumor does not resemble that of carcinoma, nor does the age of the patient suggest such a disease. The cures effected by amputation or the resection of a single bone are also against this assumption.

The summary of our investigations is also against the belief that the tumor is possibly a myeloma originating in the marrow cavity. In the first place, the elliptic area of involvement of the shaft with the bulk of tumor lying subperiosteally does not resemble the usual central and spherical contour of medullary tumors. Multiple myeloma, metastatic carcinoma and chloroma with leukemia all show a central location with a more or less spherical growth widening the medullary cavity. These tumors occupying the marrow cavity show early bone destruction and in the majority of them Bence-Jones bodies have been demonstrated during the course of the disease. Ewing's tumor, in contrast to these neoplasms, most frequently shows a narrowing or occlusion of the medullary cavity with both endosteal and subperiosteal new bone formation early in the disease, which would seem to indicate that the tumor has not a primary medullary origin. The absence of marked changes in the blood picture and Bence-Jones bodies in the urine is also against this assumption. Examination of gross specimens and microscopic sections cut transversely through the bone usually shows only a small portion of the tumor tissue in the marrow cavity; the rapid extension of the tumor in a plane parallel to the axis of the shaft indicates that the neoplasm is not able to expand freely in a central or peripheral direction, thus pointing to the fact that the growth is either intracortical or subperiosteal in origin.

The majority of the observations could be explained by either an intracortical or a subperiosteal origin of the tumor. If the neoplasm were primary in the haversian systems, this would explain the rapid infiltration of the tumor producing early endosteal and subperiosteal reactions of new bone. It would explain also the distribution of the tumor under the periosteum and into the medullary cavity in the later

stages, and account for the widening of the haversian canals and the splitting of the layers of the cortical bone so frequently observed under the microscope. However, conclusive microscopic proof for the origin of Ewing's tumor in the haversian canals is lacking. While all specimens usually show the tumor pervading these structures we have been unable to tell whether the tumor arises here or secondarily infiltrates into these channels. The assumption that Ewing's tumor arises in the subperiosteal location may be maintained with probably equal validity from the facts observed. The active subperiosteal layer which ceases at the epiphysis and atrophies in adulthood would account for the primary involvement of the shaft only, in the bones of youthful patients. This locality would account also for the fact that the bulk of the tumor is to be found under the periosteum, for the tendency of the haversian system to be infiltrated and for the reactive new bone formation of both endosteal and subperiosteal origin. It would explain also the tendency of the tumor to extend up and down the shaft rather than to form a spherical growth. It would also fit in with the absence of Bence-Jones bodies in the urine and the lack of marked changes in the blood picture.

On the basis of the observations that have just been pointed out, it is clear that whether the tumor is primarily intracortical or subperiosteal, it is evidently not medullary or primarily osteolytic, as is currently believed. The rarity of pathologic fracture, the localities affected and the results of roentgen and gross examinations are all against this assumption, and bone destruction is always a late manifestation of the disease.

Perivascular lymphatics in bone have been suggested by some as a possible source of origin for the tumor. This is not altogether unfeasible and would give this tumor an intracortical origin.[9] Although tumor cells are frequently observed about the vessels in the haversian canals, sections of normal bone do not show cells of the Ewing type from which the neoplasm might arise. While we have observed proliferation of cellular elements about these lymphatics of bone beneath such conditions as bursitis, the cells are of a different type and the endothelium of the lymphatics does not appear to us to resemble Ewing's cell. We have reviewed the endotheliomas of the soft parts along with all the sarcomas of the soft parts in the surgical pathologic laboratory and do not find a tumor duplicating Ewing's sarcoma in morphology.

The facts at our disposal at the present time do not enable us to point out either the site of origin or the histogenesis of this tumor, and while we believe that the primary focus is specific for bone and is probably intracortical or subperiosteal we prefer to leave the matter sub judice.

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9. Ewing, J.: Endothelial Myeloma of Bone, Proc. New York Path. Soc. **24**:93, 1924.

ISCHIORECTAL PROSTATECTOMY *

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Any operative procedure having as its fundamental precept the removal of a pathologic structure with due regard to its physiology and to the preservation of the related anatomy should find itself within the capabilities of every well trained surgeon.

The division of opinion of surgeons throughout the world as to the choice of method in prostatectomy indicates that except to a brilliant few neither the suprapubic nor the perineal method, with its various modifications, fulfils all requirements. The choice of one method rather than the other because of greater familiarity with the procedure and the constant attempts to vary and improve the technic are proof of a somewhat general dissatisfaction.

It was this dissatisfaction which led Voelcker, after many years' experience with both the suprapubic and the perineal methods and their various modifications, to present before the Berlin Surgical Congress, in 1919, the technic of his ischiorectal prostatectomy, with a report of fifty-six cases in which this operation was performed.[1]

He felt that the difficulties in hemostasis and in the after-care of the wound in the suprapubic operation and the technical difficulty of gaining adequate exposure by the perineal method were definite faults of these operations.

At that time, he made the following apt comparison:

> Compare for example the marked variance of our surgical principles in performing cholecystectomy and prostatectomy. When we remove a gallbladder filled with stones we do not simply loosen it from its bed by blunt dissection and then tear it in two at its neck. Rather do we carefully make our peritoneal incision, and gently free the bladder, taking the utmost care not to injure the liver and the adjoining structures. We then ligate the deeper vessels, carefully clamp and ligate the cystic duct and cover it again with peritoneum, or, when we are uncertain of the desirability of primary closure, a drain is carefully placed in proper position.
>
> In prostatectomy, however, the gland is freed by blunt finger dissection, in part not under the guidance of the eye, and is then torn from its surrounding structures.

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* From the Chirurgische Universitätsklinik und Poliklinik, Universität Halle-Wittenberg, Prof. Fritz Voelcker, Director.

1. Voelcker, Fritz: Die Prostatectomie als gut übersichtliche Operation, Ztschr. f. urol. Chir. **4**:253, 1919.

The ischiorectal method has the following distinct advantages:

1. The entire operation is done under the guidance of the eye, the anatomic structures being readily recognized and respected.

2. Exact hemostasis by means of ligature, suture and packing is possible, the bleeding points being readily seen.

3. The bladder neck and the internal sphincter are clearly seen, and so the possibility of leaving small pieces of adenoma behind is unlikely.

4. Dependent drainage from the base of the wound is obtained.

5. Death from shock has not occurred in 148 cases observed, this hazard being given by most writers as the third most important cause of death.

6. Permanent fistula or incontinence has not occurred.

The technic of the operation has been simplified in many small details in the last ten years. The procedure as described here seems not to have found its way into the American literature.

METHOD

Preparation.—Every effort is made to have the patient in the best possible preoperative condition. Preliminary drainage is made with either the indwelling catheter or the suprapubic fistula, as indicated. Preliminary vasotomy is considered an essential part of the preoperative preparation, and its performance is urged whenever possible before treatment with the indwelling catheter is inaugurated. Postoperative epididymitis is a frequent and most unpleasant complication. Young [2] reported this complication in 20 per cent, Davis [3] in 13 per cent and White [4] in 57 per cent of the prostatectomies performed by them. More than 30 per cent of a former series in this clinic developed epididymitis, but in the present series of 148 cases, all with preliminary vasotomy, this complication did not arise.

Position of the Patient.—The patient is placed in the prone position with the head and chest about 12 inches lower than the pelvis. A round leather hair pillow is placed across the lower part of the abdomen and strapped to the thighs by means of a pole running through its center; the pressure is so exerted as to force the lower abdominal organs dorsalward. The legs are widely spread about the two uprights of the operating table and the feet encased in specially constructed stirrups (fig. 1).

In my experience, the percentage of postoperative pneumonia is not increased through the use of this position. Patients who are operated on under spinal anesthesia do not complain of discomfort from the position.

Incision.—A small sponge is sewed over the anus with a purse-string suture. The incision is made over either the right or the left ischiorectal fossa, according to the preference of the operator. Usually the incision is not longer than 10 cm.,

2. Young, H.: Prostatectomy, Pre-Operative, Operative, and Post-Operative Treatment, Surg. Gynec. Obst. **36**:589, 1923.

3. Davis, Edwin: Perineal Prostatectomy, J. A. M. A. **91**:1618 (Nov. 24) 1928.

4. White, H. P. W.: Epididymitis and Supra-Pubic Prostatectomy, Lancet **202**:321, 1922.

Fig. 1.—The position of the patient. (This and the accompanying illustrations are taken from the monograph of Fritz Voelcker and H. Boeminghaus, Anatomie und chirurgische Operationslehre der Prostata, in Handbuch der Urologie, Berlin, Julius Springer, 1926, vol. 1. This is figure 25, p. 232 of the handbuch.)

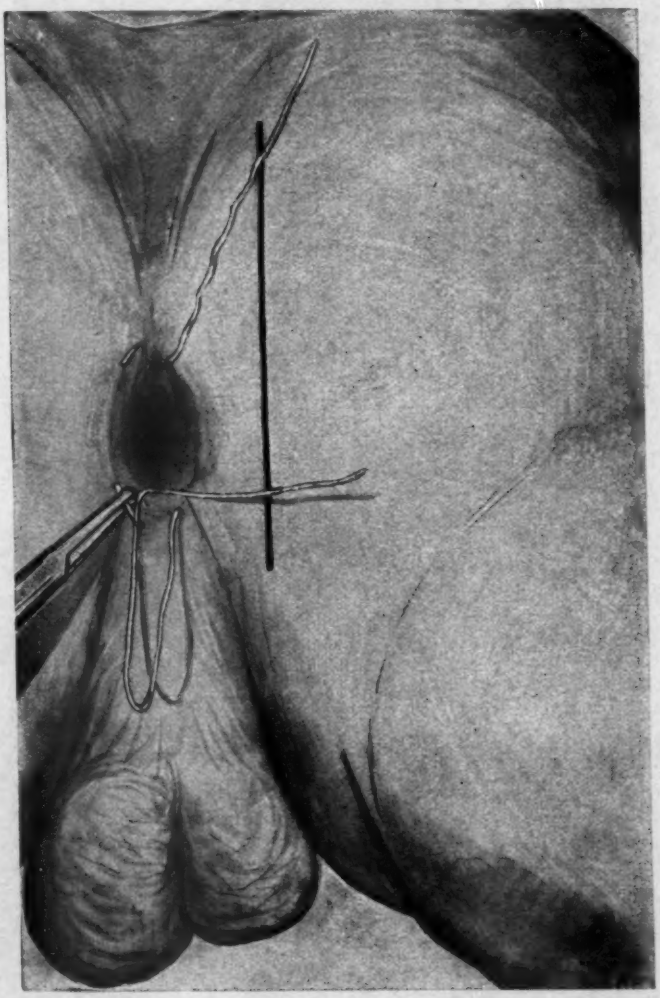

Fig. 2.—Incision.

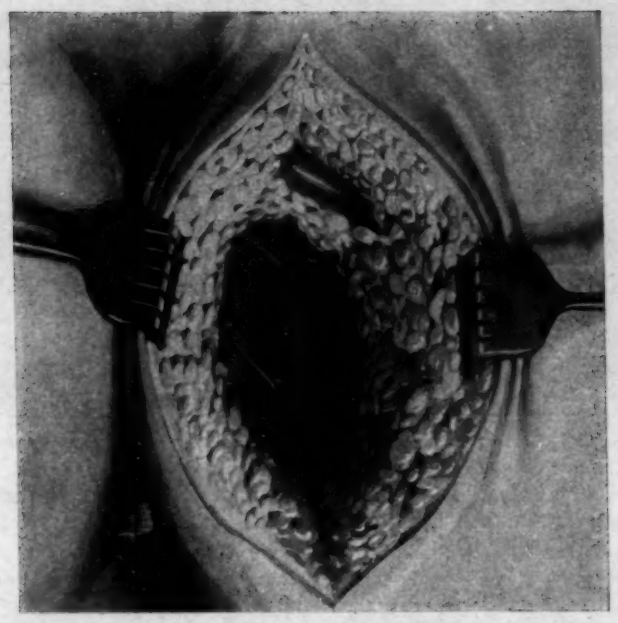

Fig. 3.—The levator ani is exposed and the direction for its incision is shown. The inferior border of the gluteus maximus is seen in the upper border of the wound (fig. 26, p. 233).

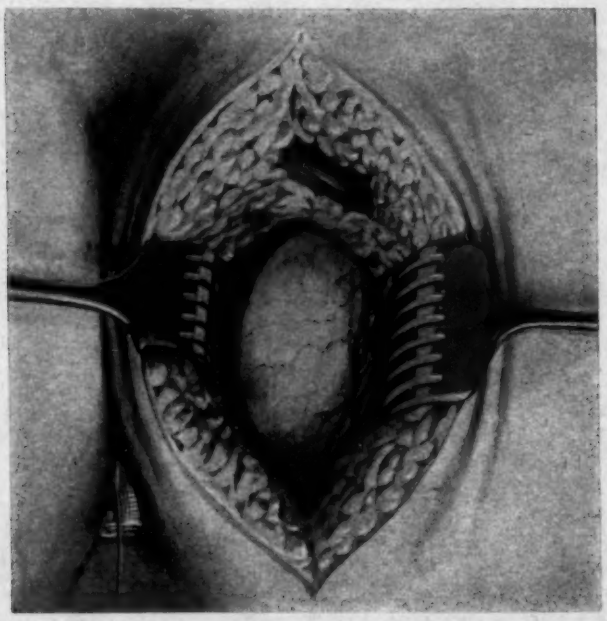

Fig. 4.—The levator ani is divided and retracted. The membrana pelvis visceralis, the accompanying venous bundle and the line of incision are shown (fig. 27, p. 233).

starting at the sacrococcygeal articulation, 3 or 4 cm. from and parallel to the midline and extending to or a little beyond the anus.

The skin and superficial fascia having been incised, the thick gluteal fat pad is divided in the same direction as the skin incision, the branches of the inferior hemorrhoidal artery being ligated as they are met. The small motor nerve branches running to the anus may be cut without fear of weakening the sphincter control. At the upper border of the incision appears the gluteus maximus, which is left untouched. The fat bolster having been incised, the levator ani muscle which lies directly beneath it is also incised parallel with the midline and retracted to either side (fig. 3). Below this muscle is the membrana pelvis visceralis, which is readily recognized by its shimmering whitish color.

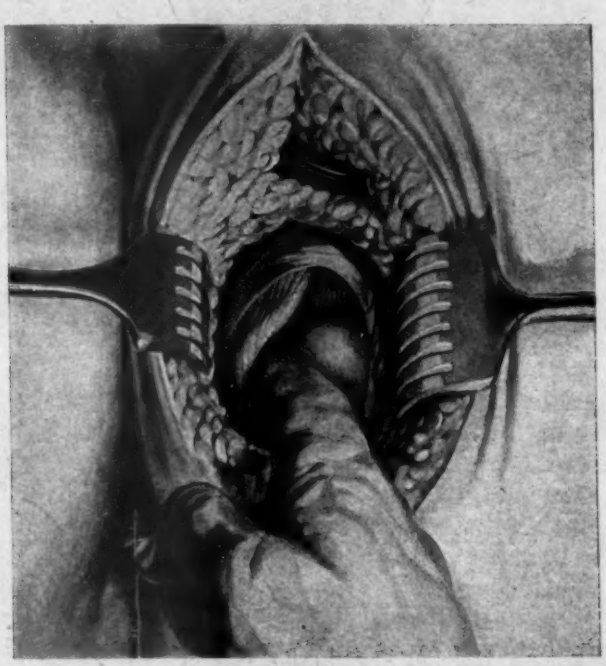

Fig. 5.—The membrana pelvis visceralis has been incised and the prostate is being separated from the rectum by blunt finger dissection (fig. 28, p. 234).

The next step may be termed the crucial one of the operation, for the deliverance of the prostate without wounding the rectum depends on the careful separation of the prostate and the rectum. These structures are bound together, from the surgical standpoint, by this rather thick layer of tough connective tissue. Fortunately, at this point there is a constant landmark in the form of a readily recognized group of veins running parallel to the anterior rectal wall. At times they lie some distance laterally and quite deep in the incision, being seen only after the cut half of the levator ani has been adequately retracted.

As these veins indicate the plane of cleavage between the prostate and the anterior rectal wall, the membrana pelvis visceralis is incised, millimeter by millimeter, slightly medial to these veins and deep enough that the incision may be widened by gently tearing this structure with the two index fingers (fig. 4).

The prostate and rectal borders are now definitely felt, and the finger is easily inserted into the plane of cleavage between them. Keeping always along the posterior prostatic surface, the operator can easily separate the anterior rectal wall from the prostate (fig. 5). The freed rectum is then retracted with a

Fig. 6.—Diagrammatic representation of the relation of the rectum and the prostate during the freeing of the latter (fig. 32, p. 237).

specially constructed, broad, sharply curved retractor, leaving the prostate in full view (fig. 6).

During this part of the operation the operator should remember that the enlarged prostate has cupped itself about the collapsed rectum, distorting it into a definitely crescentic form (fig. 7). Those who are unfamiliar with the technic may insert a light into the rectum as an added safeguard.

Fig. 7.—The rectum retractor (after Voelcker) (fig. 33, p. 237).

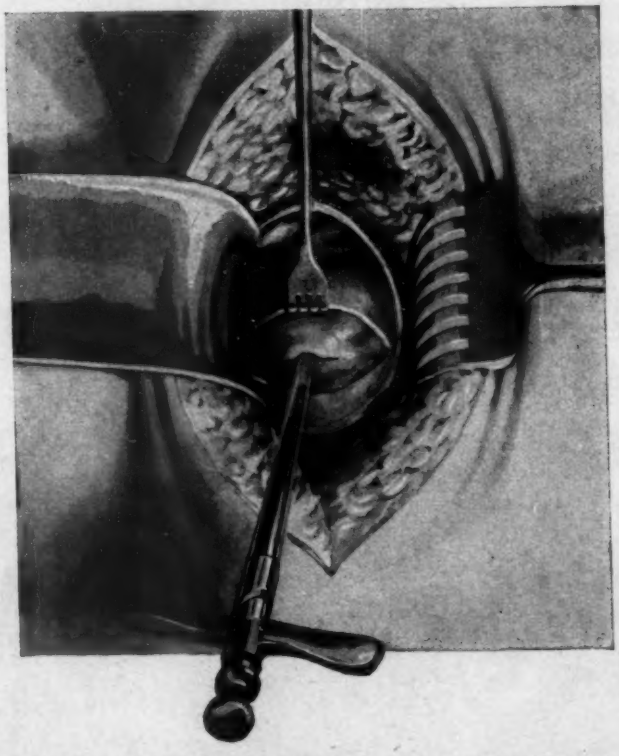

Fig. 8.—The prostatic sheath and the prostate have been divided horizontally. A Young retractor has been inserted through the prostatic incision (fig. 29, p. 235).

REMOVAL OF THE PROSTATE

A horizontal incision is now made through the prostatic sheath and the hypertrophied gland, about 1 cm. distal to its center, the incision penetrating into the prostatic urethra (fig. 8). The tip of the indwelling catheter is delivered into the wound, a Young retractor is inserted through the urethral opening, its blades are opened, and the gland is pulled gently forward and downward, the operator now recognizing the neck or base of the bladder. The prostatic sheath (the so-called capsule) is then freed with the scissors from the upper half of the divided gland until it may be held aside with a small claw retractor, the gland then being freed further by blunt finger dissection. In the region of the seminal vesicles, however, the dissection should be sharp throughout, since these structures may be readily injured by too brusque blunt dissection.

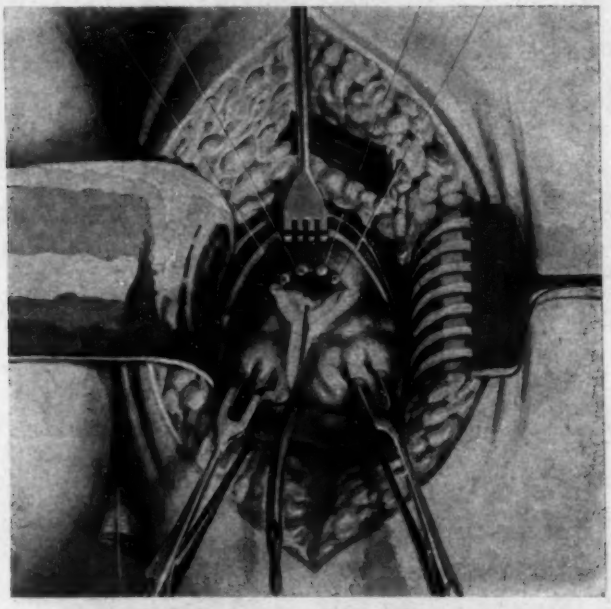

Fig. 9.—The prostate, having been divided longitudinally, is being cut from the bladder neck, sutures in the latter being laid to prevent bleeding. Grasping forceps have been substituted for the Young retractor. The indwelling catheter has been led out through the original prostatic incision (fig. 30, p. 236).

The gland is now cut from the bladder neck with the scissors, the surgeon cutting and suturing piecemeal so as to prevent bleeding (fig. 9). When the adenoma is separated from the bladder neck, it is pulled forward into the wound and cut from the pars membranacea urethra with the scalpel.

In some cases the entire procedure may be simplified if the adenoma is longitudinally divided into two halves, and a pair of forceps is substituted for the Young retractor, each half being then separately removed.

After the removal of the prostate, the inside of the bladder is cleansed and inspected. The urethral catheter is reinserted into the bladder along with a

rubber drainage tube, ½ inch (1.27 cm.) in diameter (fig. 10). The cut ends of the bladder neck and urethra may, when thought necessary, be drawn together with several catgut sutures. The wound is then packed with epinephrine gauze, the horizontal incision in the so-called capsule being sutured over a part of the tampon. The skin is then sutured, no attempt being made to unite muscle or fascia.

Postoperative Care.—Immediately following the operation the bladder is irrigated with from 150 to 200 cc. of warm salt solution. Thereafter, during the first twenty-four hours, this is repeated from every quarter to every half hour depending on the tendency to clot formation. The packing is loosened on the second day and removed on the third. The large rubber drain is removed on the

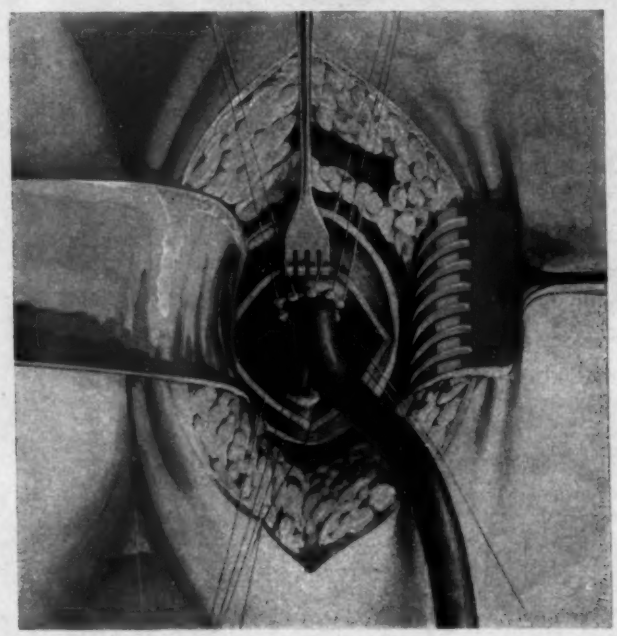

Fig. 10.—The prostate has been removed and the cut ends of the urethra and the bladder neck are being drawn together with several catgut sutures. A thick rubber tube drain lies in the bladder. The wound is now packed with gauze, the prostatic sheath being loosely sutured.

eighth to the tenth day and the urethral catheter is left in place for fourteen days except when encrustation demands earlier changing.

COMMENT

The present series includes 148 cases in which this method was used, with a mortality rate of 4.07 per cent. The age incidence was: from 60 to 65 years, 38 per cent; from 65 to 70, 28 per cent; from 55 to 60, 22 per cent; from 70 to 75, 10 per cent, and from 75 to 80, 2 per cent.

This series includes the first cases in which this method was used, eight surgeons having operated, all of whom were performing the operation for the first time. Under these conditions, it seems only reasonable to think that the next series will show a decreased mortality.

SUMMARY

1. The Voelcker method of ischiorectal prostatectomy is presented.

2. The advantages of this method are:

(*a*) The operation is done entirely under the guidance of the eye.

(*b*) Exact hemostasis by means of ligature, suture and packing is possible.

(*c*) Because of exact visibility, the possibility of leaving small pieces of adenoma behind is unlikely.

(*d*) Dependent drainage from the base of the wound is possible.

(*e*) Death from operative shock has not been encountered.

(*f*) Permanent fistulas or incontinence have not occurred.

(*g*) Postoperative epididymitis can be almost entirely controlled by the performance of vasotomy before treatment with the indwelling catheter is inaugurated.

(*h*) The series includes 148 cases in which the operation was performed by eight surgeons, with a mortality rate of 4.07 per cent.

CHOLEDOCHOGASTROSTOMY FOR SCAR TISSUE OBSTRUCTION OF THE COMMON DUCT*

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NEW YORK

Although a number of plastic operations have been done for injury to the common bile duct, a careful survey of the literature reveals that direct anastomosis of this duct with the stomach for relief of scar tissue obstruction has rarely been performed.

Eliot,[1] in 1918, in his review of the literature on the surgery of the hepatic and common bile ducts, cited six cases in each of which an anastomosis was made between one of these ducts and the stomach. In only three was the anastomosis made between the common duct and the stomach. These three cases were those of Dujarier, O'Day and Brunner.

Dujarier's and O'Day's cases are reported in this article. Eliot stated that Brunner merely noted a successful case of choledochogastrostomy and gave no details.

Kehr,[2] in 1913, said that he had united the stomach to the hepatic duct in three cases but gave no details of the operation. Eliot cited one of Kehr's cases, in which the anastomosis was between the hepatic duct and the stomach.

Dujarier,[3] in 1911, reported the case of a woman, aged 50, on whom a cholecystectomy for gallstones had been performed. Symptoms persisted, including jaundice and fever. At the second operation, the common duct was found to terminate in a cul-de-sac, above which it was much dilated. The common duct was opened and explored with the finger. It showed no obstruction above the cul-de-sac. As the opening had been made near the stomach and there were adhesions between it and the duct, an anastomosis (lateral) was performed between the stomach and the duct. Two rows of fine silk sutures were used. The anastomosis was reenforced by a fold of omentum. The patient made a good recovery and remained well for three years after operation. No digestive disturbances resulted from the discharge of bile into the stomach.

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* Submitted for publication, Nov. 12, 1929.

1. Eliot, E.: The Repair and Reconstruction of the Hepatic and Common Bile Ducts, Surg. Gynec. Obst. **26**:81, 1918.

2. Kehr: Rückblick auf 2,000 operationen an den Gallenwegen, Verhandl. d. deutsch. Gesellsch. f. Chir. **42**:273, 1913.

3. Dujarier, C.: Cholédoco-gastrostomie chez une malade opérée antérieurement de cholécystectomie, Bull .et mém. Soc. de chir. de Paris **37**:1318, 1911.

In 1920, O'Day [4] reported a case in which an operation had been performed on the patient eleven years previously. This was reported by Eliot as a "personal communication" from O'Day. In this case the patient had repeated attacks of colic, followed by persistent jaundice. At operation, "a fistulous tract was found leading from the perforated duct to the lesser peritoneal cavity, which was shut off from the foramen of Winslow. In the lesser cavity was found a considerable amount of bile containing one calculus. During an attempt to free the choledochus it broke off at a point just above the adherent mass in which the termination of the duct was embedded, and abundant bile exuded from the proximal end. An anastomosis was done between this stump and the anterior wall of the stomach in its lower one-third." Eleven years after operation, the patient was in excellent health, with no digestive disturbances. O'Day said that in this case, implantation of the stump of the duct into the stomach seemed the best and safest way out.

In 1927, Matthews [5] reported a case as a "choledochogastrostomy" in which symptoms had recurred after a cholecystectomy for gallstones. Jaundice was marked. At operation the hepatic duct was found greatly dilated and adherent to the duodenum, with a small opening into the duodenum. This fistula was closed. The opening into the hepatic duct was just at the junction of the right and left hepatic ducts. Bile and "sandlike stones" were found on exploration with the finger in each duct, and were removed. Then an anastomosis was made to the upper anterior surface of the stomach just proximal to the duodenum. The anastomosis was done by a suture method in two rows, much like gastro-intestinal anastomosis. This procedure in itself gives some idea as to the size of the dilated ducts. The patient made a good recovery, and has been well since the date of operation, July 28, 1924. (The anastomosis in this case was apparently between the hepatic duct and the stomach, although the designation of the operation would indicate that it was between the common duct and the stomach.)

Walters,[6] in 1929, reported seventeen operative cases of benign stricture of the common or hepatic duct. He said that he had found anastomosis of the common or hepatic duct to the duodenum the most satisfactory type of operation in such cases, provided that sufficient duct remains proximal to the stricture to permit anastomosis. In his tabulation of cases, he included two in which choledochogastrostomy was done. He did not describe the technic of this operation. In both

4. O'Day, J. C.: Surgery of Ductus Communis Choledochus, Ann. Surg. **71**:293, 1920.

5. Matthews, A. A.: Choledocho-Gastrostomy, M. Sentinel **35**:152, 1927.

6. Walters, W.: Strictures of Common and Hepatic Bile Ducts, Surg. Gynec. Obst. **48**:305 (March) 1929.

cases cholecystectomy had been done elsewhere, but jaundice and pain had developed subsequently. In one case there was a stricture of the common and hepatic ducts and a stone in the hepatic duct. Choledochogastrostomy was done, and a T-tube was placed in the common duct. The immediate results were good, and the tube was passed. Jaundice and fever, but no pain, recurred within a year. In the second case, the patient died of intra-abdominal hemorrhage twelve hours after operation.

REPORT OF CASE

History.—A woman, aged 48, was admitted to the Post-Graduate Hospital on June 25, 1929, with the complaint of jaundice, itching of the skin and pain in the epigastrium for the past few weeks, with increasing jaundice and itching.

The patient was operated on for abdominal tumor in 1919, for goiter in 1925, and for disease of the gallbladder in October, 1928. Otherwise the history was unimportant.

Present Illness.—The patient dated her complaints to four weeks before examination, when she noticed that her skin was becoming yellow and that she had some discomfort in the epigastrium. There was no severe pain but an uncomfortable sensation in the upper part of the abdomen, accompanied by belching without vomiting. Her condition gradually became worse. For the last ten days she had been bothered by itching of the entire body, as well as by increasing jaundice. She said that in October, 1928, she was operated on in Chicago for a condition of the gallbladder, after which there was drainage of bile until the early part of January, 1929. Then the wound healed, and she remained in fairly good health until about one month before admission to the hospital, when she began to have epigastric discomfort and jaundice; at that time she consulted her family physician, who ordered that a series of roentgenograms of the gastro-intestinal tract be made; these were negative. The report from the previous operation was as follows: Operation revealed the stomach and the duodenum to be normal. The gallbladder was green and thickened. There were enlarged glands along the duct; no stones were palpated. Examination of the appendix showed adhesions around the cecum, with subacute inflammation. The uterus was normal in size and position. The adnexa showed adhesions. A cholecystectomy and an appendectomy were performed.

Physical Examination.—The patient was thin and undernourished, with markedly jaundiced skin and sclera. She said that she was 20 pounds (9 Kg.) underweight. Her neck showed a scar from an operation for goiter but no evidence of thyroid enlargement. There was a firmly healed scar over the upper right rectus muscle and also a firmly healed lower midline incision. As a result of scratching, the patient had numerous abrasions over the arms, legs and body, with pruritus ani.

Laboratory Data.—Urinalysis gave negative results. The bleeding time was four minutes; clotting began in five and one-half minutes and was complete in six minutes. The white blood count and the differential count were normal.

The diagnosis was biliary obstruction from scar tissue.

The patient was given daily hypodermoclysis: 1,000 cc. of 3 per cent dextrose and 15.5 grains (1 Gm.) of calcium chloride, intravenously, for four days.

At operation on July 3, 1929, the abdomen was opened through a right rectus incision, the previous scar being excised. When the peritoneum was opened,

Fig. 1.—Dilated common and hepatic ducts. *A* represents the site where incision was made in the stomach and the common duct.

Fig. 2.—First row of sutures approximating the stomach to the common duct. *A* shows a second row of posterior sutures; next the operator will continue the anterior row.

Fig. 3.—The anterior row of sutures is completed; three mattress sutures are taken between the stomach and the liver.

Fig. 4.—The mattress sutures are tied approximating the stomach to the under surface of the liver.

moderate adhesions were found in the right upper quadrant in the region of the gallbladder bed, but the gallbladder bed could be exposed without much difficulty, and the stomach was freely movable; the duodenum was adherent and definitely fixed. When the common duct was exposed a definite scar tissue obstruction was found 1 inch (2.54 cm.) below the hepatic veins, with a dilatation of the upper inch of the common duct and both hepatic veins. The common duct was opened, and the right and the left hepatic veins were probed and found to be patent (fig. 1). The common duct was definitely obstructed by scar tissue. The stomach could be easily approximated to the dilated portion of the common duct (fig. 2). It was impossible to approximate the doudenum to the common duct. A direct anastomosis between the common duct and the stomach was done, the steps of which were identical with the steps of a gastro-enterostomy. After completion of the anastomosis, three mattress sutures were taken from the stomach to the under surface of the liver to relieve any tension on the suture line between the common duct and the stomach (figs. 3 and 4). A small rubber tissue drain was inserted through the peritoneum. The abdomen was closed in anatomic layers.

Postoperative Course.—The patient's convalescence was uneventful for the first few days. There was no leakage of bile around the drain until the fourth day, when the dressing was saturated with bile. On the fifth day, there was only slight leakage of bile on the dressing, and on the sixth day it entirely disappeared. The cigaret drain was removed on the sixth day, and from then on there was no leakage of bile. At this time, it was noticed that the jaundice was definitely subsiding and the itching diminishing. The patient continued to improve, and was discharged from the hospital on the twentieth day. At that time she was practically free from jaundice, and itching had entirely disappeared. The wound had healed, with the exception of a slight area at the lower angle which was infected.

The patient was last seen on Nov. 11, 1929, at which time she felt perfectly well and was free from jaundice. She had gained 18 pounds (8 Kg.) in weight since the operation.

COMMENT

The one reason for doing this operation was the ease with which the stomach could be approximated to the common duct for the anastomosis, without tension on the suture line.

125 East Seventy-Second Street.

THE REPAIR OF CLEFT PALATES AFTER UNSUCCESSFUL OPERATIONS

WITH SPECIAL REFERENCE TO CASES WITH AN EXTENSIVE LOSS OF PALATAL TISSUE *

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If one is a young man and somewhat of a surgical optimist, a review of the measures used in operations on cleft palates is apt to temper one's enthusiasm somewhat, and one may entertain a great many doubts as to the probability of surgical intervention ever attaining its ultimate goal—the ideal functional result— so far as the cleft palate is concerned. In the past many of the great minds in surgery, as a glance at the names which represent the real milestones of progress will reveal, have wrestled ardently with the problem of cleft palate.

In 1764, Le Monnier,[1] a French dentist, reported the first successful repair of a cleft velum. Later, his success was followed by von Graefe [2] of Germany in 1817, Roux [3] of France in 1819 and Warren [4] of America in 1820. But it remained for Dieffenbach to report the first successful closure of both the hard and the soft palate in 1834. Baizeau [5] in 1853 and von Langenbeck [6] in 1861 claimed originality for the operation of Dieffenbach with its lateral incisions. But even today, the operation bears the name of von Langenbeck.

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* Submitted for publication, Sept. 7, 1929.

* From the Surgical Department of the University of Kansas School of Medicine.

* Read before the Section on Surgery, at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 10, 1929.

1. Le Monnier, quoted by Robert: Memoires sur different objet de medicin, Paris, Masson & Cie, 1764; quoted by Verneuil, A. S. S.: Memoiries de chirurgie, Paris, Masson & Cie, 1877-1878, vol. 1, p. 506.

2. Von Graefe, C.: Die Gaumennaht, ein neuentdecktes Mittel gegen angeborene Fehler der Sprache; J. d. Chir. u. Augenh. **1**:556, 1820.

3. Roux, P. J.: Memoires sur la staphyloraphie, Arch. gén. de méd. **7**:516, 1825.

4. Warren, John C.: On an Operation for the Cure of Natural Fissure of the Soft Palate, Am. J. M. Sc. **3**:1, 1828.

5 Baizeau, quoted by Verneuil, A. S. S.: Memoires de chirurgie, Paris, Masson & Cie., 1877-1878, vol. 1, p. 506.

6. Von Langenbeck, B.: Operation der angeborenen totalen Spaltung des harten Gaumens nach einer neuen Method, Deutsche Klinik **12**:231, 1861; Weitere Erfahrungen im Gebiete Urano-plastik mittelst Ablösung des mucösperiostalen Gaumenüberzuges, Arch. f. klin. Chir. **5**:1, 1864.

Fergusson has generally received credit for first advocating the severance of the palatal muscles (1845) [7] and also with osteotomy (1873) [8] of the horizontal processes of the palatal bones for relaxation. It appears, however, that Froriep [9] first carried out the former procedure in 1823, and Dieffenbach [10] the latter procedure in 1826. Billroth,[11] in 1861, made the suggestion that the hamular processes be fractured to relieve tension. The use of the mucosal flap from the septum to aid in the repair of the fissure was done first by Lannelonque [12] in 1877. The "criss-cross flap" operation of Davies-Colley [13] for closure of the hard palate appeared in 1890. In 1893, Brophy [14] suggested the wiring operation for bringing the separated alveolar ridges together at an early age. Finally, in 1902, the Lane [15] operation appeared which was an extension of the principle of the Davies-Colley flaps to both the hard and the soft palate.

THE USUAL OPERATIVE PROCEDURES

Practically all the common operations for the repair of complete cleft palates, such as the Lane, Warren and von Langenbeck, have a more or less common fundamental defect. When the palate is being repaired, the mucoperiosteal flaps have to be separated from the palate bones and brought down nearly to a horizontal level to obtain midline closure because the elevation of the horizontal plates of the palate bones on both sides are like the two sides of a raised drawbridge. Thus the upper surface of the freshly repaired hard palate is raw, and as granulation occurs the soft tissues of the hard palate either come up to the horizontal plates or the plates go down to the soft tissues. Probably

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7. Fergusson, William: Observations on Cleft Palate and on Staphyloraphie Tr. Med. Soc.-Chir. **28**:273, 1845; On Cleft Palate and on Staphyloraphie, Med Times **16**:25, 1847; On Hare-Lip and Split Palate, Lancet **1**:719, 1864.

8. Fergusson, William: A New Operation for Cleft Palate, Lancet **11**:784, 1873; Successful Treatment of Four Cases of Cleft in the Hard Palate by a New Operation, ibid. **1**:298, 1874.

9. Froriep: "Nottizen" chirurgische Kupfertafln, Weimer, 1823.

10. Dieffenbach, J. F.: Chirurgie Erfahrung, 1834, no. 324, p. 168; Die Operative Chirurgie, Leipzig, F. A. Brockhaus, 1845.

11. Billroth, T.: Ueber Uranoplastik, Wien. klin. Wchnschr. **2**:241, 1889.

12. Lannelonque: De l'uranoplastic osteo-muqueuse, Bull. et mem. Soc. de chir. de Par. **111**:467, 1877.

13. Davies-Colley, T. N. C.: On a Method of Closing Cleft of the Hard Palate by Operation, Brit. M. J. **11**:950, 1890.

14. Brophy, T. W.: Brophy's Operation for Cleft Palate, in Catching: Comp. Pract. Dent. Atlanta, 1894, vol. 258, p. 262; Proc. Third Internat. Dent. Cong. **152**:153, 1900; quoted by Stone, in Bryant and Buck: American Practice of Surgery, New York, William Wood & Company, 1908, from Park: Surgery, Philadelphia, Lea Brothers & Company, 1893.

15. Lane, W. A.: On Cleft Palate, Lancet **11**:433, 1902.

both movements occur to some extent, especially in the young, but the tendency for the anterior end of the soft palate to be pulled up to the apex of the V formed by the posterior edges of the horizontal plates of the palate bones is always present.

The observance of a few cases of narrow recessive deformity of the upper jaw in the adolescent who has undergone an operation in infancy in whom the alveolar ridges were wired together warns one to let the maxillary bones alone if possible. Thus the Brophy wiring operation, which necessitates a later operation of the Warren type, is losing adherents. When the surgeons who still adhere to the belief that the early wiring together of the alveolar ridges is a good procedure are excluded, opinion is fairly uniform as to the operative methods to be used and to the necessary essentials preceding closure of the cleft palate in which sufficient tissue is present. In selected cases the Lane operation may be useful, yet because of the likelihood of a slough of the upper flap and the probabilty that the cicatrix will interfere with mobility of the velum, it is not generally popular. The Warren operation without the lateral incisions gives good results in palates with high vaults and in palates in which the arch of the alveolar ridge has been narrowed by a wiring operation. The von Langenbeck operation with its lateral relaxing incisions, loosening of the raphe at the posterior end of the palatal bones and the preservation of the posterior palatine artery to each flap seems to have withstood the test of time for the routine case and probably is justly the most popular operation for the usual cleft palate.

PALATE LENGTH NECESSARY

Aside from its function of forming a diaphragm between the nasopharynx and oropharynx in the act of swallowing, the palate normally should be able to form a "flap valve" between the resonating cavities of the nose and the mouth at the moment of the proper articulation of a great many of the consonants—all except m, n and ng. In "cleft palate" speech some of the air which in the articulation of nearly all consonants ought to be expelled through the mouth escapes through the cleft into the nose, where it vibrates in the nasal cavity and finally escapes through the anterior nares. The oral consonants are converted into the voiced nasal consonants and cannot be voiced as loudly, as clearly or as forcibly as they should be.

Thus one of the outstanding needs in surgical intervention of the cleft palate today is a workable procedure which effectually lengthens the soft palate. With this hypothesis in mind, a few clinical experiments were performed on badly damaged palates with the hope that the way to some improvement of the present-day results might become somewhat clearer. The hope was entertained that these badly damaged palates might show sufficient functional improvement after operation to

warrant the extension of the same methods to the ordinary case of cleft palate in which operation was not performed or the case in which operation had been done with failure to obtain midline union in which no tissue loss had occurred. As yet, however, the justification for such an extension of the type of operations to be described has seemed questionable.

THE SEVERELY DAMAGED PALATE

Besides patients with the ordinary types of cleft palate in which operations were not performed or the cases in which operations were performed with failure to obtain midline union, but in which no tissue loss has occurred, a number of patients present themselves for repair who have been operated on one or more times previously and in whom there is unmistakable evidence of an old slough. An occasional patient is also seen who shows a marked disuse atrophy of the soft palate which was due to the fact that an operation was not performed at the proper time.

To show the interrelation and to aid in discussion, the severely damaged palates have been divided into three groups, as follows: 1. Cases in which midline union is probable or has occurred but in which the velum is markedly atrophic or definitely shortened by cicatrix. 2. Cases in which after operation the tissue of the hard palate is preserved so that the closure of the hard palate has been obtained or is obtainable, but in whom a considerable part of the velum has been lost. 3. Cases in which a previous operation has resulted in a sloughing of so much of the tissue of the hard palate and of the soft palate that repair is obviously impossible without the use of tissue from other sources than the mouth.

The obvious need in the palates of the first group is the addition of tissue without interference with mobility so that the velum can come in contact with the posterior pharyngeal wall. In palates of the second and third groups, any soft tissue diaphragm built in to take the place of the soft palate or the whole palate, respectively, which does not obstruct breathing ought to be an aid in closing off the nasopharynx from the oropharynx in the act of articulation.

Most of the patients selected were of the type for whom the usual methods of operation had little to offer. In each case the procedures used for repair, it seemed reasonable to believe, would replace the palatal tissue loss. The results obtained thereby are presented by brief histories of the cases.

REPORT OF CASES

The report of the case that follows represents an effort to solve by operation the problem of the patient with an almost complete loss of the velum (group 2). It was obviously impossible to repair such a palate without tissue other than that from the palate.

CASE 1.—On Nov. 21, 1926, a woman, aged 21, was admitted to the Bell Memorial Hospital with the history of four unsuccessful operations on the palate.

From a point opposite the level of the larynx a long pedicled flap of mucosa, about 6 cm. in length by 3 cm. in width, was dissected upward off the posterior pharyngeal wall in the midline so that the base of the flap was about on a level with the posterior edge of the palate. The flap could then be pulled forward to the posterior edge of the hard palate. From the remnants of the upper surface of the soft palate a semicircular flap was loosened with a right angled knife and turned downward and toward the midline so that the mucosal covering was adjacent to the tongue. This procedure left a large raw area on the upper surface of the remnants of the velum. The pharyngeal flap was then sewed into this raw defect. Thus a mucosal covering was made for the upper surface of the soft palate. The flaps from the remnants of the soft palate then were drawn to the midline beneath the pharyngeal flap and the edges were sewed together (figs. 1, 2 and 3).

On the day following the operation it was noticed, to my great surprise, that the patient articulated her words nearly perfectly. Her

Fig. 1 (case 1).—Diagram of the upper surface of the soft palate, showing method in which the "shelf" flaps were turned medialward and the position of the pharyngeal flap after it was thrown into the raw area on the upper surface of the palate.

speech was improved so startlingly that prematurely the conclusion was reached that the key to the problem of defective speech in cleft palate had been found. But as the flap from the pharyngeal wall gradually tubed itself, although the freedom of the airway improved, her speech was somewhat less perfect. This patient has been followed up for two and a half years. When she has a cold she has some respiratory difficulty because of accumulated discharge in the nasopharynx, especially at night. Her speech is a little thick and reminds one of speech when the mouth is too full of food, but the "cleft palate" type of speech has been remedied. The improvement in the articulation of her words is really remarkable (fig. 4).

In case 2 an attempt was made to improve speech by lengthening the short atrophic velum. This soft palate was typical of the type seen in which operation is postponed until adult life (group 1). A fairly

Fig. 2.—Lateral midsection view of the palate, pharynx and pharyngeal flap after it was sewed on the upper surface of the soft palate as in case 1.

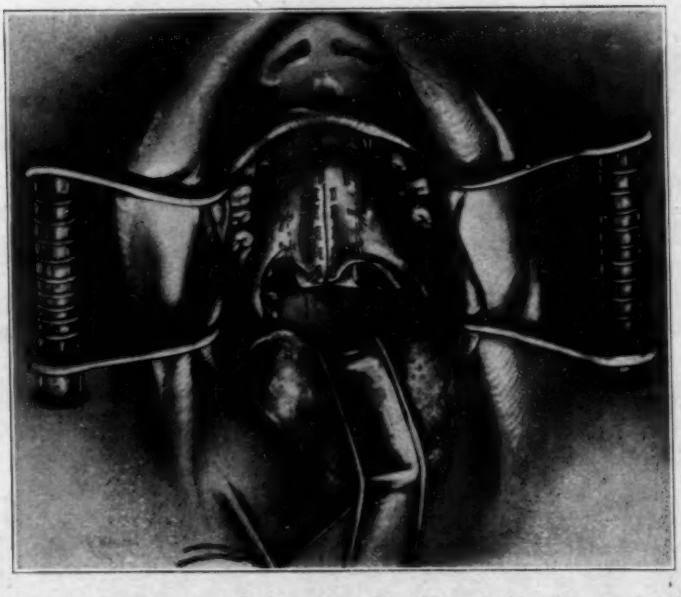

Fig. 3.—The appearance of the soft palate from inside the mouth after the pharyngeal flap was sewed to the upper surface of the soft palate as in case 1. (In cases 2, 3 and 4, the methods of turning the flaps were reversed because the latter operation is easier to perform mechanically.)

marked disuse muscle atrophy of the velum was present, but there was sufficient palatal tissue to come together in the midline.

CASE 2.—On Dec. 19, 1928, a man, aged 23, entered the Bell Memorial Hospital with a complete cleft of the velum. A pharyngeal flap was turned downward instead of upward and thus the flap was attached on the under surface of the new velum instead of on the upper surface as in the preceding case. The method of placing the flap in this case was reversed, because technically it is easier to raise the semicircular shelf of flap on the soft palate from the mouth side than from the nasal side (figs. 5 and 6).

Six weeks later, the pharyngeal flap was detached from the posterior pharyngeal wall. The tail of the flap was cut rather long so that it could be turned over on the upper surface of the velum and doubled on itself to make a thick mass of tissue as wide and as long as possible.

Fig. 4 (case 1).—Photograph of the inside of the mouth; taken on July 5, 1929.

This patient has been followed up for about eighteen months. He is an intelligent person and practices speaking consonants daily with the aid of his wife, who detects changes in sound better than he. Improvement in the articulation of his words is definite.

Following the operations in the first two cases, in February, 1927, a case was reported by Kirkham[16] in which he sutured together the superior constrictor muscle of the pharynx at the sides of the pharyngeal cavity. Speech was nearly normal during the three days that the stitches held. Kirkham was led to believe that the shortening of the loop of the superior constrictor muscle was significant and had more of a bearing on correct articulation than heretofore had been thought.

16. Kirkham, H. L. D.: Preliminary Paper on Improvement of Speech in Cleft Palate Cases, Surg. Gynec. Obst. **44**:244, 1928.

Passavant [17] long ago called attention to the hypertrophy of the superior constrictor muscles of the pharynx in the patient with cleft palate. Overdevelopment of the superior constrictor muscle is explained on the basis of its being the only muscle in articulation utilized by the patient with cleft palate to close off the nasopharynx from the oropharynx.

It seems reasonable to attribute some of the improvement in speech experienced by the patient in case 1 to a tendency of the superior constrictor loop of muscle to be pulled forward somewhat by the flap which connects the velum with the posterior pharyngeal wall. More significant than the tendency of the forward pull, however, and applicable whether the pharyngeal pedicle flap is severed or not, is the narrowing of the pharynx obtained because of the removal of the central mucosal strip.

The third case is an example of rather marked cicatrical contracture of the soft palate with some muscle atrophy (group 1). The hard palate was closed completely except for a small hole in the midline. The velum was separated to within about 1 cm. of the hard palate, was badly scarred and was shortened, and some of it appeared to be missing.

CASE 3.—This patient was 2½ years old when first seen in Bell Memorial Hospital. Two operations had been performed previously. He was operated on on Jan. 16, 1928. The velum was rebuilt by the utilization of a pedicled flap from the posterior pharyngeal wall. The pharyngeal flap was turned downward and placed beneath the raw surface formed by the turned up flaps from the soft palate, as in case 2 (figs. 5 and 6).

This boy's speech shows improvement; however, he is apparently subnormal mentally, and it is difficult to judge accurately the amount of improvement. He has been followed up for eighteen months. His mother thinks that the improvement in speech has been definite. The pedicled flap still remains attached to the pharyngeal wall.

The patient in case 4 had suffered from about as much loss of the tissue of the soft palate as the one in case 1, and falls in group 2 of my classification.

CASE 4.—This patient was operated on on Aug. 28, 1928, in Bell Memorial Hospital, when 3½ years of age. He had had three previous attempts at closure of the palate. More than one half of the soft palate had sloughed. The hard palate, however, was closed. A shelf of mucosa from the remnants of the soft palate was turned upward with the mucosal surface toward the nasal cavity. By swinging a flap from the posterior pharyngeal wall with the pedicle downward to the raw surface of the upturned flaps from the soft palate, a new soft palate of good length and width was constructed, as in cases 2 and 3 (figs. 5 and 6).

17. Passavant, G.: Ueber die Beseitigung der naselnden Sprache bei angeborenen Spalten des harten und weichren Gaumens; Arch. f. klin. Chir. **6**:333, 1865.

Fig. 5.—Medial cross-section view of the method used when the pharyngeal flap is turned downward. (In cases 2, 3 and 4 the methods of turning the flaps were reversed, as shown in figures 5 and 6 because the procedure is easier to perform mechanically.)

Fig. 6.—View of the palate from within the mouth when the pharyngeal flap is turned downward instead of upward.

Improved articulation in this patient was immediate and fairly marked. He has been observed for ten months. The pharyngeal flap has not been detached from the pharyngeal wall.

PREVIOUS IDEAS ON PALATE LENGTHENING

In 1876, Schoenborn [18] advocated the use of a flap from the posterior pharyngeal wall. In 1878, Passavant tied the uvula to the posterior pharyngeal wall by turning small flaps so that raw surface would be to raw surface. The idea was not accepted with enthusiasm, although it was admitted that speech was improved. Sedillot [19] criticized the idea on the basis that surgeons had known that in cases of stricture between the nasal and buccal cavities the nasal type of speech remained. Again, recently, Rosenthal [20] utilized a flap from the posterior pharyngeal wall to repair the velum. Von Kuster's [21] lengthening operation by means of a portion of the detached edge of the cleft also belongs to this group.

In 1922, Blair [22] performed an operation in which flaps from the cheek were outlined and turned in through the lateral incisions on the upper raw surface of the palate anterior to the upper mucosal surface of the velum to increase the mucosal covering of the upper surface of the palate. This operation lengthens the upper surface of the palate and probably allows the velum to drop down a little.

In 1925, Dorrance [23] described an operation for the lengthening of a palate in which the soft tissue of the hard palate and the raphe of the soft palate are loosened from the horizontal plates of the palatal bones. An encircling incision was made within the alveolar margins and both the hard and the soft palates were displaced backwards. Again, Limberg,[24] in 1927, and Lvoff,[25] in 1928, presented somewhat similar methods. In these operations, even if the flaps of the hard palate did retain their blood supply, it would seem probable that the raw surface

18. Schoenborn: Ueber eine neue Methode de Staphlorhaphie, Arch. f. klin. Chir. **19**:528, 1876.

19. Sedillot, C., quoted by Christopher Heath, in John Ashhurst: The International Encyclopedia of Surgery, New York, William Wood & Company, 1889, vol. 4, p. 911.

20. Rosenthal, W.: Pathologie und Therapie der Gaumendefelste, Fortschr. Zahnh. **4**:1021, 1928.

21. Von Kuster: Den Operation der complizierten Hasenscharte, Zentralbl. f. Chir. **32**:713, 1905; Ueber die Operative Behandlung der Gaumenspalten, Arch. f. klin. Chir. **46**:215, 1893.

22. Blair, V. P.: Personal communication to the author.

23. Dorrance, George M.: Lengthening of the Soft Palate in Cleft Palate Operations, Ann Surg. **82**:208, 1925.

24. Limberg, A.: Innovations in Operative Methods, Zentralbl. f. Chir. **54**: 1745, 1927.

25. Lvoff, P. P.: Operation for Lengthening Palate, Vestnik khir. **13**:212, 1928.

between the upper mucosal surface of the velum and the posterior edge of the horizontal plates of the palate bones would simply scar and pull the soft palate back to its former position.

In one of my recent cases (1929) the upper surface of the junction of the hard and soft palates was relined with cheek flaps, as in the operation of Blair, to obtain length of the upper surface of the palate, and the whole palate was pushed back, as in Limberg's operation, to obtain length of the lower surface. This operation appears logical.

NEARLY COMPLETE LOSS OF PALATAL TISSUE (GROUP 3)

In persons in whom only remnants of both the hard and the soft palates remain after operations in which a slough has occurred, a substitute for palatal tissue can be built from tubed pedicled flaps from either the neck or the arm. The paramount question is whether or not a complete new palate built in with inert tissue is of enough functional value to compensate the patient for his trials during a tedious operative procedure.

The brief abstracts of the three cases that follow outline the methods by which such difficult palates can be repaired and give some evidence of the difficulties to be overcome. These cases fall in group 3 of the classification.

In case 5 the young woman had had several previous operations due to which at least one half of the tissue of the hard palate was absent and practically all of the tissue of the soft palate had sloughed. The tissue loss in this case seemed too great to allow a successful repair by the method of a posterior pharyngeal flap alone. It was decided to use a tubed pedicled flap from the left arm.

CASE 5.—A girl, aged 17, was admitted to the Trinity Lutheran Hospital on July 15, 1928. On July 16, the flap was raised from the arm and tubed. On the under surface of the upper end of the flap, which was the part to go into the mouth, a full thickness skin graft was applied. A full thickness skin graft was sewed into the defect on the arm left after the flap was raised. About a week later the upper end of the flap was detached.

On July 28, the flap was sewed in the defect of the palate after shelf flaps were turned upward from remnants of the old palate. A flap was also raised from the posterior pharyngeal wall and sewed to the upper surface of the distal end of the flap that had just been placed in the mouth. A block was wired between the teeth to prevent her from biting the flap, and a cast was applied to the head and arm to hold them in proper position. Twelve days later the pedicle of the flap was cut across and the cast removed. One week later, the proximal end of the flap in the mouth was smoothed out and united to the anterior hard palate (figs. 7, 8, 9, 10 and 11).

The girl was intelligent. She had led her class in high school, but because of the defect in speech caused by the palate, she attempted to get along in the world by saying only "yes" and "no," smiling and shaking

her head. After the palate was repaired she began to try to talk, and although articulation was imperfect she did show improvement. She is now diligently attempting to overcome her defect in speech by self-training.

When this patient's palate was examined on July 15, 1929, to my surprise it was noted that the new palate contracted and moved. The tissue in the midline, although incapable of movement itself, had evi-

Fig. 7.—The flap one week after it was raised from the arm. At the upper end on the under surface a full thickness skin graft was grown. (This is not visible, however.) Beneath the gauze a full thickness skin graft, which is not visible because of gauze, was sewed into the defect caused by the removal of the flap.

dently been rendered taut by the attachment of the remnants of the palatal muscles at the sides so that when the muscles contracted the whole soft palate showed movement. At this time her speech was remarkably improved. The posterior tip of the new palate was still attached in the midline to the posterior pharyngeal wall. This will be detached at a later date so that the effect on speech can be observed.

Fig. 8.—The methods of turning the shelf-flaps from the sides of the palatal tissues and from the posterior pharyngeal wall. The flap from the arm is then sewed well back into the mouth and put in contact with the raw surfaces.

Fig. 9 (case 5).—The inside of the mouth after the operation was finished. Note that the pharyngeal flap is sewed to the tail of the skin flap from the arm, and the "shelf flaps" of mucosa have been turned upward above the skin flap from remnants of tissue at the side of the palate.

The patient in case 6 had had several previous operations on the palate and practically all of the palate had sloughed. Because of the discomfort of an arm cast, I chose to use a flap from the neck. His alveolar ridge was cleft, so I planned to grow the flap to the lip so that the end

Fig. 10 (case 5).—A photograph of the plaster cast and flap as thrown into the mouth from the arm.

Fig. 11 (case 5).—Appearance of patient a few months after operation.

beneath the chin could be detached and passed through the cleft. Thus the discomfort of a mechanism to keep his mouth open would not be necessary.

CASE 6.—A boy, aged 2 years, was admitted to Bell Memorial Hospital on Nov. 15, 1928. A flap was raised from the neck and wall of the upper part of the chest with its base beneath the chin. Twelve days later the distal end of the flap was turned upward and attached beneath the upper lip. Thus a "jump flap" was made of it. About this time the patient developed influenza and ran a fever for about a week. It was suggested to his mother that she take him home at this time. However, as she was somewhat sensitive about his appearance, he was kept at the hospital. He should have gone home at this time for a long rest and complete recovery. On Feb. 8, 1929, the "jump flap" with its pedicle beneath the upper lip was turned into the mouth through the cleft alveolar ridge. The flap grew perfectly, but considerable trouble was experienced in getting the child to eat. He had practically a normal temperature after the first two or three days following the operation. Laboratory observations were negative except for a hemoglobin of 50 per cent. A transfusion was given, after

Fig. 12 (case 6).—Appearance of patient after the flap had been raised from the neck.

which he began to eat a little and sit up in bed. On the evening of February 20, twelve days after operation, the nurse took him in her arms and gave him a feeding, after which she left the ward. She returned in about fifteen minutes and he was dead. No autopsy could be obtained.

The exact cause of the boy's death remains uncertain, but a lesson should be learned. He should have been given two or three months' rest to improve his condition before the flap was placed in the mouth. Perhaps it might have been better judgment to have postponed the operation until the child was several years older (figs. 12, 13 and 14).

The patient in case 7 was 21 and had undergone several operations on the palate in babyhood after which the hard and soft palates had sloughed almost completely.

Fig. 13 (case 6).—A drawing of the flap after it had been attached beneath the upper lip and its raw surface had been grafted by the Thiersch graft.

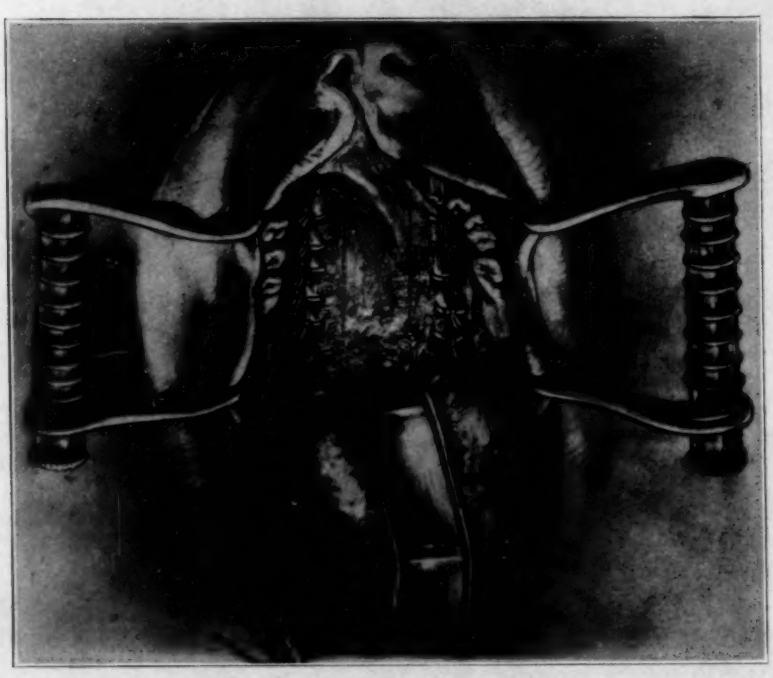

Fig. 14 (case 6).—A drawing of the "jump" flap after it had been severed from the neck and turned in to build the new palate. Note the side "shelf" flaps and the posterior pharyngeal flap turned on the upper surface of the skin flap.

CASE 7.—On June 17, 1929, in Trinity Lutheran Hospital, a flap was raised from the left arm and tubed. On July 2, the flap was placed in the mouth in a manner similar to that used in case 5. On the second night after operation, a tracheotomy was done because of laryngeal edema.

For a few days following the tracheotomy he had a temperature of 103.5 F. which gradually subsided. After two weeks, the flap was cut next to the arm

Fig. 15 (case 7).—Appearance of patient after the flap had been sewed into the mouth. The patient's mouth is held open by a triangular edge of wood which is wired between the teeth.

Fig. 16 (case 7).—As much of the new palate as could be shown by a photograph, two months after operation.

and the plaster fixation was removed. Two days after this he was sent home for two weeks. After this time he reentered the hospital to have the anterior end of the flap smoothed out and attached within the alveolor curve. He left the hospital five days later (figs. 15 and 16).

It is possible that a tracheotomy should be a part of this operation, unless an experienced nurse is in constant attendance. If a tracheotomy is not made at the time of the original operation, the instruments necessary to do a tracheotomy should be kept at the bedside for the first few days. At the present time (Sept. 20, 1929) this patient is at work and his speech is nearly normal. The nasal tone has disappeared from his speech. The posterior part of his palate moves slightly when he swallows or speaks. The flap is still attached to the posterior pharyngeal wall in the midline.

PREVIOUS USE OF PEDICLED SKIN FLAP

The idea of the repair of a palatal defect by a flap from elsewhere than inside the mouth is rather ancient. It was first unsuccessfully attempted by Blasius [26] by the use of a flap from the neck. Thiersch,[27] in 1867, and Rotter,[28] in 1869, used the principle successfully. Later the method was successfully used by von Eiselberg [29] and Blair.[30]

SUMMARY

By the use of a pedicled flap from the posterior pharyngeal wall a method is presented which will lengthen somewhat the short velum without narrowing the nasopharynx or oropharynx sufficiently to interfere with the function of breathing or swallowing. The lengthening of the velum and the narrowing of the oropharynx obtained have improved speech and aided particularly in the articulation of the oral consonants in the persons so far observed. A pedicled flap from the posterior pharyngeal wall can be used in the successful reconstruction of a diaphragm of tissue between the nasopharynx and the oropharynx and is particularly applicable to those cases in which a considerable part of the velum has sloughed. In the past, such persons have usually been advised that surgical intervention has nothing to offer. The results reported definitely contradict the truth of such a hopeless verdict. The functional results in this group (group 2) are particularly satisfactory and hopeful. It is possible to use the pedicled flap from outside the mouth to repair this type of palate, but the procedure necessitates several operations and is far more difficult for both the patient and the surgeon.

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26. Blasius, quoted by von Eiselberg, Frederick: Zur Technik der Uranoplastik, Arch. f. klin. Chir. **64**:509, 1901.

27. Thiersch, C.: Verschluss eines Loches un harten Gaumen durch die weichtheile der Wange, Arch. f. d. Heilkunde **9**:159, 1868.

28. Rotter, Julius: Deckung eines Defectes un harten Gaumen mittelst eines Sternlappens, München. med. Wchnschr. **36**:535, 1889; Plastische Operation an der Mundhöhle und in der Nase, Verhandl. d. deutsch. Gesellsch. f. Chir., 1889.

29. Von Eiselberg, F.: Zur Technik der Uranoplastik, Arch. f. klin. Chir. **64**:509, 1901.

30. Blair, V. P.: Operative Treatment of Difficult Cases of Palate Defects After Infancy, Surg. Gynec. Obst. **12**:289, 1911.

For the repair of the palate in which most of the tissues of both the hard and the soft palate have sloughed (group 3), a pedicled flap of skin and subcutaneous tissue from the arm or neck can be used. Obviously sufficient tissue to repair this extensive defect must be obtained elsewhere than from inside the mouth. Although the tediousness of this procedure is admitted, the results in the preceding cases indicate that a diaphragm of skin and subcutaneous tissue is better than no palate or an obturator and is distinctly worth while. The movement of the new palate obtained after transplantation of a flap from the arm (cases 5 and 7) gives proof of the ability of the remnants of the palatal muscles which are attached at the sides of the new palate to move the central flap somewhat. The amount of this movement will probably depend on the amount of good muscle available for insertion at the sides. Thus the principle of the application of a pedicled flap from outside the mouth to repair a gross loss of palatal tissue places at the surgeon's command a final method, by the use of which, it can be said with truth, a defect of the cleft palate does not exist in which surgical intervention has nothing to offer, provided enough tissue remains within the alveolar curve to serve as a raw base of sufficient width to obtain union after the skin flap is sutured in place.

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ABSTRACT OF DISCUSSION

DR. FREDERICK A. FIGI, Rochester, Minn.: I believe that the ingenious procedure which Dr. Padgett has presented for taking care of some of the difficult postoperative cleft palates, that is, the use of a flap from the posterior pharyngeal wall, is a real contribution. This should prove of decided value in taking care of some of the bad postoperative cases. At the Mayo Clinic, in the ordinary run of primary cases of cleft palate, our routine procedure has been the von Langenbeck operation to which he referred. Those patients presenting unusually wide defects, whether primary or due to postoperative loss, are taken care of with the two-stage delayed flap operation described by New in 1922. This consists of elevating the soft tissues on either side of the defect by means of a long lateral incision just inside the alveolar border. The double pedicled flap thus formed is crowded toward the midline by means of an iodoform gauze pack on either side. After from five days to a week the margins of these flaps are pared and sutured. In cases presenting still wider defects, an attempt is made to close the hard palate only in this manner at the first series of operations, the soft palate being closed by a similar two-stage procedure after several months. The length of the lateral incisions does not appear to have a direct bearing on subsequent palatal function, even in those cases in which the incisions are extended laterally around the tuberosity and well back into the commissure. Transforming the tensor palati into a levator by breaking off the hamular process of the external pterygoid plate, as suggested by Dorance and others, also at times assists in securing relaxation without subsequent interference with function. Multiple stage operations must of course be attended by the production of a greater amount of scar tissue and thereby increased rigidity of the palate. However, we have seen no appreciable difference in the function of palates closed in this manner in comparison with those in which we have secured primary union.

This multiple stage operation will permit of closure of many of the bad postoperative cases in which primary closure is entirely out of the question. I believe that this should be tried in preference to the use of a flap from the posterior wall if it appears at all advisable, for a closure obtained in this way will give an incomparably better functioning palate than one into which inert tissue has been introduced. Personally, I cannot become enthusiastic over the use of cutaneous flaps for the closure of wide palatal defects, even though the case may be hopelessly inoperable otherwise. The advantage of the introduction of this inert mass of tissue into the palate appears questionable to me in view of the difficulties associated with the operation and the hazards involved in comparison with the ease of closing such a defect satisfactorily with an artificial velum.

CYSTIC CIRRHOSIS OF THE BREAST*

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The occurrence of cysts in the female breast is common. Some of these cysts develop, apparently, from distended lactiferous ducts (galactocele). They are comparatively unimportant and are not puzzling from either a morphologic or a clinical point of view. The presence of multiple, often small, cysts in the gland tissue proper of the breast is of far greater importance. The interpretation of their nature and histogenesis has been studied by a great number of authors, yet no consensus has been arrived at. This is demonstrated sufficiently by the large number of names given to this condition. The confusing nomenclature includes, among others, the following terms: polycystic breast, cystic disease, polycystoma, hydrocystoma, cystic epithelioma and epitheliofibrosis of the breast.

The main questions that arise in studying this condition concern the histogenesis of the cysts, the nature of their matrix, the character of the epithelial proliferation and its relationship to neoplastic conditions and, finally, the part played by the stroma in the development of the process.

A short survey of the literature will show the divergence of opinion concerning these questions.

REVIEW OF THE LITERATURE

Astley, Cooper and Langhans [1] were among the first to study cystic disease of the breast, but the first extensive studies of this subject were those of Réclus [2] (1865-1888) who described the disease as "maladie cystique des mamelles." His examinations were so important, particularly from a clinical point of view, that later writers referred to this disease as "maladie de Réclus." His description and that of all the later authors agree in one point, that there is an abundance of connective tissue in the breast with hyalinization of the fibers and a varying amount of spindle and round cells in between. With the

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* From the Department of Laboratories, United Israel Zion Hospital.

1. Langhans: Virchows Arch. f. path. Anat. **58**:137, 1873.

2. Réclus: Rev. de chir., 1865, p. 761; Clin. chir. de la Pitié, 1883; Gaz. d. hôp., 1887, no. 83; Rev. de chir., 1888, p. 248.

increase of this fibrosis, the lobules become more and more separated and the glandular parenchyma more and more scattered. Compression of the epithelial elements by the fibrous tissue is often predominant; the compressed glandular acini are often cut off from their lactiferous duct (Hertz, Ingier,[3] Langhans, Samelson).

While the importance of fibrosis is universally accepted, its pathogenesis has been attributed to various causes. The first author who suggested its development from an inflammatory process was König[4] (1880), who referred to the condition as "mastitis chronica cystica." In France, Trellat and Trillaux[5] brought forth a similar conception, while Phocas and Quenu[6] compared the mammary lesion with the cirrhosis of the liver or the kidneys which they also believed to be of inflammatory origin. They coined the name "cirrhose épithéliale mammaire."

Those who advocated the inflammatory theory relied on the presence of round cell infiltration, the cellularity of the connective tissue in the earlier stages and occasionally on the abundant presence of leukocytes. The changes of the epithelial tissue elements were considered merely as secondary to the inflammatory process and were compared to similar lesions in other glandular organs subjected to chronic inflammation (Haeckel, Maly, Glannan,[7] Rohloff,[8] Lichtenhahn[9]). Other authors who believed in the inflammatory conception, such as Borst, Cornil[10] and Delbet,[11] stressed the diffuse nature and the frequently bilateral occurrence of the condition, its occasional combination with adenomatous growth and the early participation of the epithelium in the proliferation.

Even those authors who believed in the inflammatory character of the disease and held that the process starts primarily in the connective tissue had to admit the striking character of the epithelial changes. The development of multiple and often large cysts with metaplasia and finally stratification of the epithelium and of active proliferation with abundant mitoses was so suggestive that many investigators felt inclined to class these changes with neoplastic processes.

While Réclus, Langhans and others explained the cysts by mechanical distention of the acini, Brissaud assumed that active proliferation of the epithelium was the cause of cyst formation and classified the

3. Ingier: Virchows Arch. f. path. Anat. **198**:338, 1909.
4. König: Zentralbl. f. Chir., 1893, vol. 3.
5. Trellat and Trillaux: Rev. de chir., 1888.
6. Phocas and Quenu: Rev. de chir., 1888.
7. Glannan: South. M. J. **2**:806, 1909.
8. Rohloff: Deutsche Ztschr. f. Chir. **54**:106, 1900.
9. Lichtenhahn: Deutsche Ztschr. f. Chir. **90**:507, 1907.
10. Cornil: Tumeurs du sein, Paris, 1908.
11. Delbet: Traité de chirurgie de Le Dentu et Delbet, 1899, vol. 7.

disease as a neoplasm ("épithéliome cystique intra-acineux"). Sicre [12] shared his opinion and was the first to emphasize that, although cystic disease of the breast is a benign tumor, it is noteworthy for its potentiality to malignant degeneration. The neoplastic conception was stressed particularly by Schimmelbusch, who claimed that the essence of the process was the proliferation of the epithelium, which fills up the acini and is followed by disintegration in the center, thus forming cysts. Production of connective tissue between the lobules of the breast gland is only secondary and of no real importance. The condition based on active epithelial proliferation and characterized by formation of cysts would justify the name of cystadenoma of the breast. A large number of later investigators accepted Schimmelbusch's [13] point of view (Keibel,[14] Saar,[15] Tietze,[16] Goens,[17] Hahn,[18] Silverra). Most of these authors stressed the intensity of the epithelial proliferation which often goes beyond simple hyperplastic or even adenomatous conditions, and would justify the assumption that they already belong to precancerous changes.

An intermediary position was taken by Askanazy,[19] who emphasized the importance of the fibrosis and held that the connective tissue also participates in the process of proliferation. He recommended the name "epitheliofibrosis cystica." Other authors, such as Sasse, suggested the possibility that both neoplastic and inflammatory changes concur in the development of the cystic disease.

To summarize briefly, those who believe that the disease is of inflammatory origin base their contention on the following arguments: the presence of round cell infiltration, leukocytes and plasma cells; cellularity of the connective tissue in the early stages, desquamation of the epithelium and diffuse and even bilateral distribution of the changes. As cause of the inflammation, they accept either bacterial infection or some unknown irritation.

Those who favor the neoplastic origin stress the importance of the epithelial proliferation with its tendency to metaplasia and finally to malignant degeneration. They consider the changes of the stroma as secondary and unimportant.

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12. Sicre: De la maladie cystique de la mamelle, Thèse de Paris, 1890.
13. Schimmelbusch: Arch. f. klin. Chir. **44**:117, 1892.
14. Keibel: Berl. klin. Wchnschr., 1904, p. 808.
15. Saar: Arch. f. klin. Chir. **84**:223, 1907.
16. Tietze: Deutsche Ztschr. f. Chir. **56**:512, 1900; **75**:117, 1904.
17. Goens: Contribution a l'étude de la glande mammaire sénile et de ses états précancéreux, Thèse de Génève, 1919, no. 881.
18. Hahn: Virchows Arch. f. path. Anat. **262**:531, 1926.
19. Askanazy: Schweiz. med. Wchnschr. **55**:1017, 1925; Beitr. z. path. Anat. u. z. allg. Path., 1923, vol. 71.

In opposition to both theories, a third conception has been brought forth by a large group of other investigators. Already Bard and Lemoine [20] believed that a congenital weakness of the tubular structures accounted for their distention by a slightly increased intraglandular pressure. They called the condition "essential cystic disease of the breast." The developmental theory was more seriously substantiated by the extensive contributions of Krompecher,[21] who emphasized the similarity of certain cells, quite common in the lesions in the breast, to those of the axillary sweat glands. He also claimed that these sweat glands and the breast gland proper are of similar origin in the embryo, while they develop into two different types of glands later. He claimed that groups of glands of the sweat gland type may develop erroneously within the breast tissue and are responsible for the formation of the cysts with those peculiar "pale cells." Krompecher distinguished two stages of the disease: the first with preponderant connective tissue formation and comparatively few small cysts (fibrosis hydrocystica), the second characterized by a large number of more extensive cysts which obscure the development of fibrosis in the stroma (polycystoma hydrocysticum). Krompecher's views are shared in many respects by Aschoff [22] who preferred, however, the name of mastopathia cystica and claimed that irritations, due to physiologic stress but also to pathologic factors, are responsible for this condition.

Cystic disease of the breast has been compared also to the hyperplasia of the prostate in senile persons (Bloodgood [23]), but this comparison does not solve the problem and does not seem to be a lucky one, as the cystic disease of the breast occurs at a much earlier period of life. The conception, however, that a process of involution might be responsible for the epithelial changes as well as for the fibrosis seems quite suggestive (Speese and Konjetzny [24]). That involution might be influenced by the lack of hormonic stimulation or by some other endocrine dysfunction is actually conceivable, but could not be substantiated (Pribram,[25] Moskowitz,[26] Dietrich and Kuckens [27]).

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20. Bard and Lemoine: Arch. de méd., 1890.

21. Krompecher: Beitr. z. path. Anat. u. z. allg. Path. **62**:403, 1916; Virchows Arch. f. path. Anat. **250**:495, 1924.

22. Aschoff: Ergebn. d. allg. Path. u. path. Anat. **2**:515, 1897.

23. Bloodgood, J. C.: Ann. Surg. **79**:172, 1924; Pathology of Chronic Cystic Mastitis of Female Breast, Arch. Surg. **3**:445 (Nov.) 1921; Bull. Johns Hopkins Hosp., April, 1921; Diagnosis of Early Breast Tumors, J. A. M. A. **81**:875 (Sept. 15) 1923.

24. Konjetzny: Zentralbl. f. Chir. **50**:1760, 1922; Med. Klin. **16**:180, 1921.

25. Pribram: Deutsche med. Wchnschr. **45**:1075, 1919.

26. Moskowitz: München. med. Wchnschr. **74**:874, 1927; Arch. f. klin. Chir. **144**:138, 1927.

27. Kuckens: Beitr. z. path. Anat. u. z. allg. Path. **80**:40, 1928.

A large number of other authors like Bertels,[28] Mintz,[29] Todyo,[30] Lukowsky,[31] Marchand,[32] Lexer and Theile stressed the point that the cystic disease is neither inflammatory nor neoplastic and starts essentially as a hyperplastic condition of the connective tissue with secondary, mostly mechanical, interference within the glandular elements. Strangulation of the acini and ducts accounts for the obstruction of the ordinary discharge, retention and cyst formation. Subsequent irritation yields inflammatory changes and hyperplastic proliferation of the epithelium.

Other authors, particularly Judd,[33] Rodman,[34] Castle, Custone, Porter,[35] Glannan and Hart,[36] were more conservative in their statements and refrained from offering any definite conclusion as to the pathogenesis of the disease; yet they all emphasized the tendency of this condition to develop into a malignant process.

SUMMARY OF AUTHORS' CASES

From the study of our own cases and in summarizing the observations, we could construct the following picture: Constant features of the disease are fibrosis of the breast gland and cystic dilatation of some of the glandular structures. Other changes are less constant, and their presence or absence seems to be dependent on the state of development in which the diseased breast was removed and examined histologically. It seems to us that the early stages of the condition are characterized by regressive changes of the breast gland which consist of atrophy, on the one hand, and vacuolization and occasional desquamation, on the other. Proliferation of the stroma in between the epithelial structures is quite common, but not at all constant (cases 100, 180, 460, 1066, 5266 and 5550.)

The second stage in the development of the condition seems to be represented by active proliferation of the epithelial cells. The proliferating cells are larger and conspicuous for a more intensely staining cytoplasm. The staining is decidedly basophilic. This proliferation may set in in glandular units which were not distended previously during the regressive stage; this yields almost solid epithelial nests or

28. Bertels: Deutsche Ztschr. f. Chir. **124**:9, 1913.

29. Mintz: Berl. klin. Wchnschr., 1899, p. 1029.

30. Todyo: Arch. f. klin. Chir. **104**:440, 1914.

31. Lukowsky: Deutsche Ztschr. f. Chir. **157**:81, 1921.

32. Marchand: München. med. Wchnschr., 1916, p. 396.

33. Judd: J. Michigan M. Soc. **13**:11, 1914.

34. Rodman: Diseases of the Breast with Special Reference to Cancer, Philadelphia, P. Blakiston's Son & Company, 1921.

35. Porter: Surg. Gynec. Obst. **1**:400, 1905; **31**:584, 1920.

36. Hart, Deryl: Intracystic Papillomatosis, Tumors of the Breast, Benign and Malignant, Arch. Surg. **14**:793 (April) 1927.

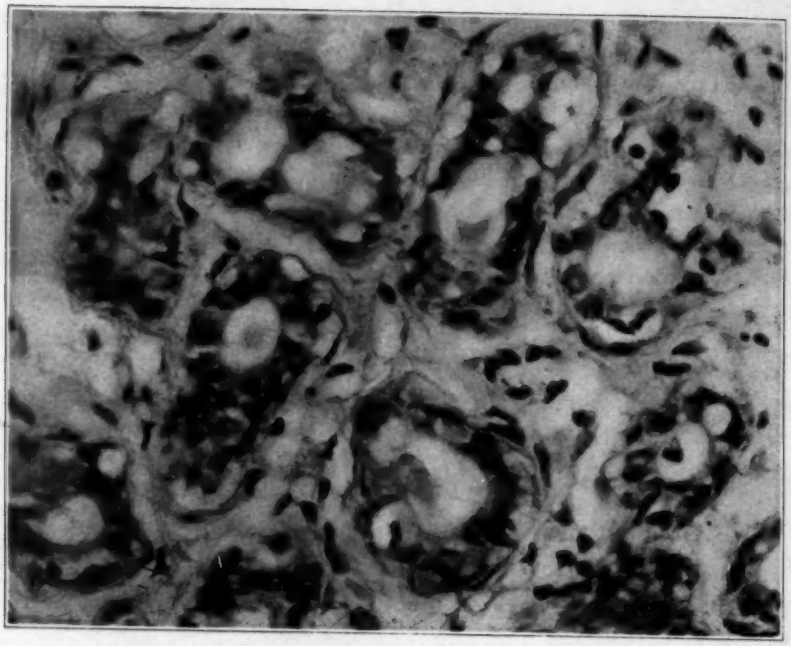

Fig. 1.—Vacuolization and incipient dilatation of breast gland acini.

Fig. 2.—Incipient cystic dilatation of breast gland acini.

alveoli. It occurs, however, just as frequently in previously distended tubules, but does not necessarily develop all over their circumference. In such cases one side of the small cyst is lined with flat epithelium, whereas the rest shows multiple layers of larger cells with basophilic staining. The regressive changes, of course, do not subside with the onset of proliferation, and combination of the two is common (cases 354, 460, 468, 500, 606, 671, 700, 1000, 1041, 1066, 1278, 5221 and 12,976).

Further development of the lesion progresses on two main lines, one of which is the formation of larger cysts, whereas the impression of the

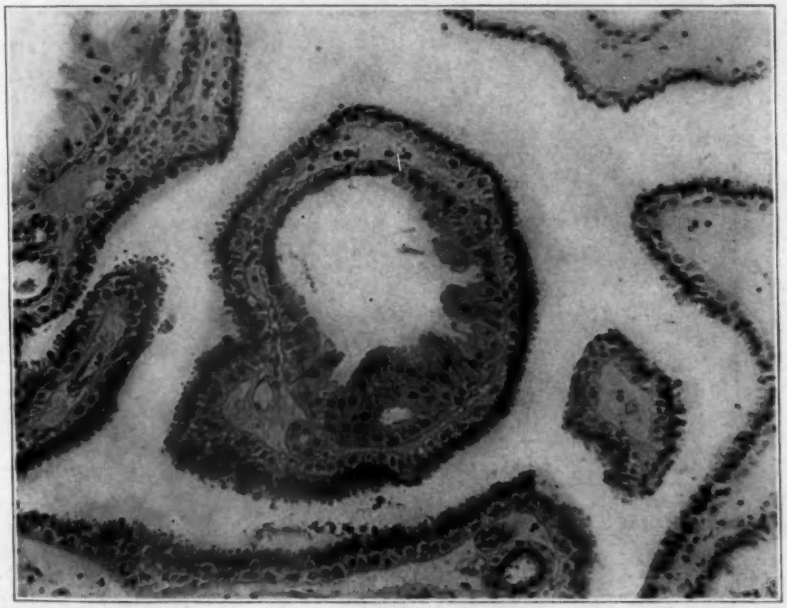

Fig. 3.—Development of eosinophil epithelium from ordinary epithelium in papillary cystadenoma.

other is more that of a hyperplastic process of the glandular parenchyma. In the larger cysts and occasionally also in the smaller ones, we are impressed by the appearance of large epithelial cells with eosinophil cytoplasm. These cells usually form a single layer, in contradistinction to the other cysts in which at least two layers can be distinguished. These cells are usually quite regular, cuboidal or of high columnar shape. Active proliferation of these cells is expressed by real papilli or more frequently by pseudopapilli without any vascular or connective tissue support (cases 53, 460, 500, 1328, 5221 and 5266). These eosinophil or pale cells, as they are often referred to, are of a fairly homogenous structure; more frequently, however, it is readily visualized

that the eosinophil substance forms intracellularly into small granules or lumps which coalesce later. Part of this hyaline substance is frequently expelled from the cell and found in the lumen as globular hyaline material (cases 215, 606, 1066, 1200, 1278, 5266 and 5550). It is quite common to see cysts of various size with comparatively low lining epithelium which, however, reveals digit-like expansions toward the lumen. These cells already show the onset of intracellular hyalinization, particularly in their expansions, which break off readily. Hyaline globules found in cysts without typical eosinophil epithelium develop from such cells as were first described.

Fig. 4.—Large cyst lined partly with eosinophil cells and partly with ordinary low cuboidal epithelium.

It is fairly easy to demonstrate a constant line of development from the ordinary lining cell of the cysts over the small cell with digit-like expansion to the fullfledged eosinophil cell. It can be demonstrated also that in one and the same cyst part of the lining cells are of the eosinophil type, whereas the rest consist of ordinary or extremely flattened epithelium. Moreover, one can demonstrate lobules of breast gland tissue in which part of the lobule preserves its ordinary structure, while the rest show some simple cysts and others eosinophil cells. Solid nests consisting of eosinophils are occasionally encountered in such lobules.

Proliferation in the diseased breast gland tissue reaches a remarkable degree in the advanced stages of the condition. The result is the formation of solid alveoli or more often of small cysts with multi-

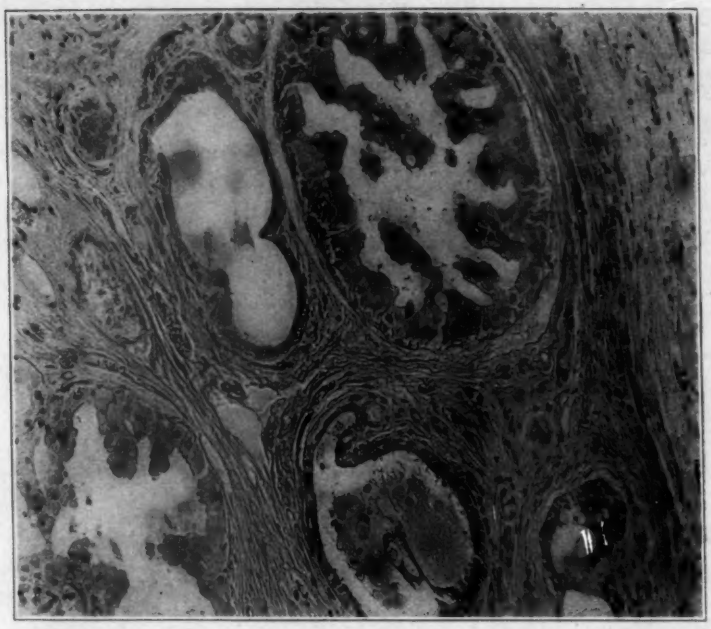

Fig. 5.—Multiple cysts, some with eosinophil, others with ordinary, epithelium or intermediary cells. Numerous papilli in the eosinophil cysts.

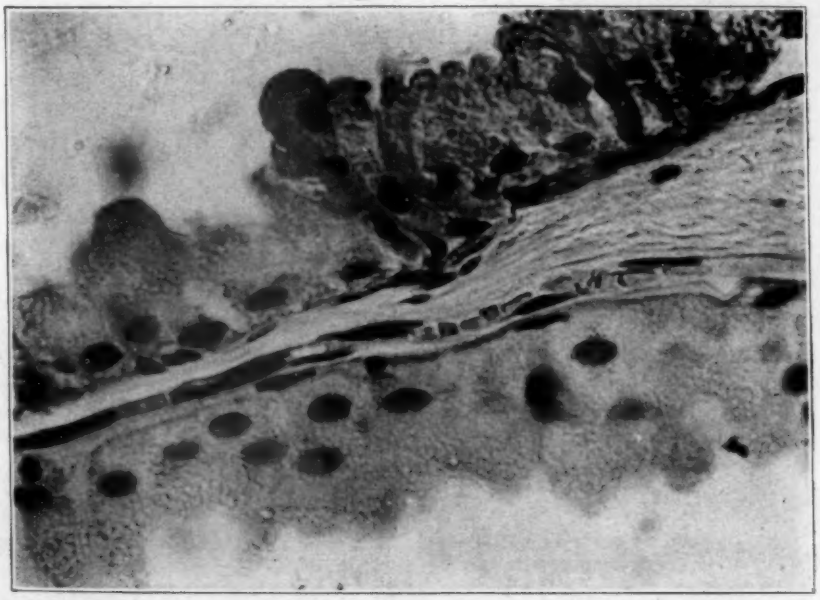

Fig. 6.—Septum between two adjacent cysts with eosinophil lining. Spindle-shaped cells at the base of the epithelium enclose capillary spaces which contain red blood cells.

layered epithelium from which peculiar trabeculae spread across the lumen and form a delicate network, until finally the open spaces between these proliferating cells disappear completely (cases 53, 354, 500, 570, 606, 1000, 5221, 5266 and 12,976). Distended cysts with flat, apparently not proliferating, epithelium, papillary cysts, or cysts with trabeculation in their lumen and finally solid alveoli often occur together within the area occupied previously by a single breast gland lobule. Of course, in this stage of proliferation the epithelial growth is not always confined to its original area, and coalescence of several adjacent lobules occasion-

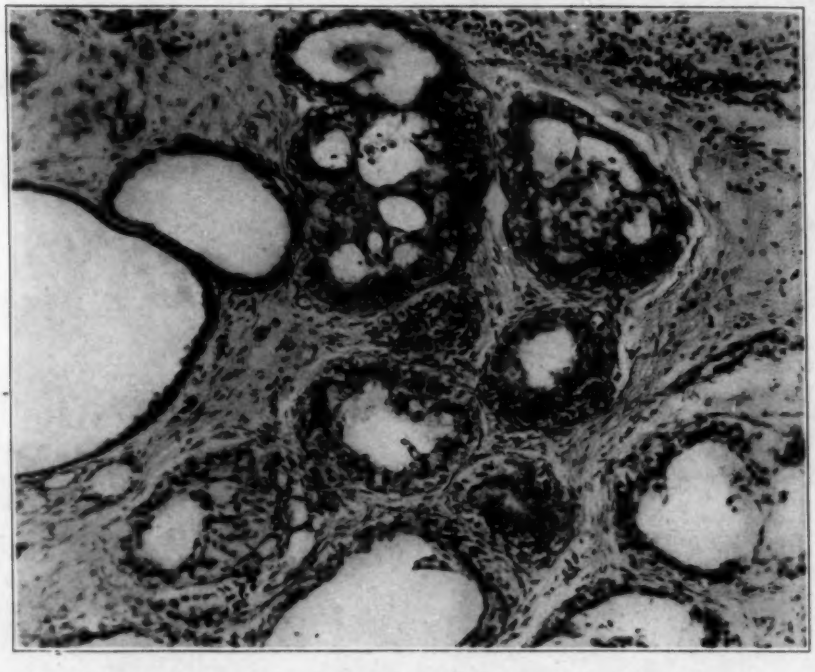

Fig. 7.—Multiple cysts; hyperplasia of the epithelium with trabeculation.

ally produces quite extensive masses with little stroma in between. The amount of stroma is reduced further by coalescence of adjacent cysts. This happens, as it does in many other organs, if the septum between two contiguous cysts is thinned out until it breaks through, whereby the two cysts unite. Remnants of the former septum project into the lumen of the cyst as small spurs.

Extensive hyperplastic vegetation of the cystic breast gland is not always easily distinguished from a neoplastic condition, and a satisfactory classification of the lesion is altogether impossible. It is more a matter of taste, whether one calls the lesion a papillary cystadenoma or cystic hyperplasia. Remnants of fat tissue or atrophic islands of

breast gland embedded in hyaline fibrous tissue in between the papillary cystic structures are suggestive of a hyperplastic condition rather than of an adenomatous neoplastic process.

In some of our cases, well circumscribed and morphologically well characterized benign neoplasms were present (cases 606, 1000, 1066, 5266, 1750, 1857 and 1932). In two cases the neoplasms were pure adenomas, while in the others, they belonged plainly in the group of ordinary fibro-adenoma. It is impossible to decide whether the origin of these neoplasms had anything to do with the cystic disease of the

Fig. 8.—Hyperplastic breast gland with proliferating epithelium.

breast gland; the presence of the tumors may have been merely incidental.

Mammary carcinoma was more frequent in our material (cases 53, 354, 500, 570, 741, 1908, 4000, 5273, 5550, 7010, 11,010 and 12,976, and the character of the changes observed seems to point to a certain relationship between the hyperplastic processes in the breast gland and the later development of carcinoma. In some of the cases the carcinoma was fairly cellular and alveolar in structure, yet the formation of cysts within the carcinomatous alveoli was quite conspicuous. The carcinomatous nature of these tumors was unquestionable, in view of their infiltrative growth and the morphologic appearance of the cells. Still

there were areas in which the anaplasia of the tumor cells was not so distinct and in which the resemblance to the hyperplastic forms of the cystic breast gland appeared particularly striking. In the midst of the cancer tissue were cysts lined with flat epithelium or with flat epithelium on one side and solid groups of tumor cells on the other. Transitions between the two cell types were common. They and the general structure of the tissue excluded the possibility that we were dealing with an invasion of the preexisting cysts by cancer cells. Other areas of the same breast showed changes which were certainly not neoplastic

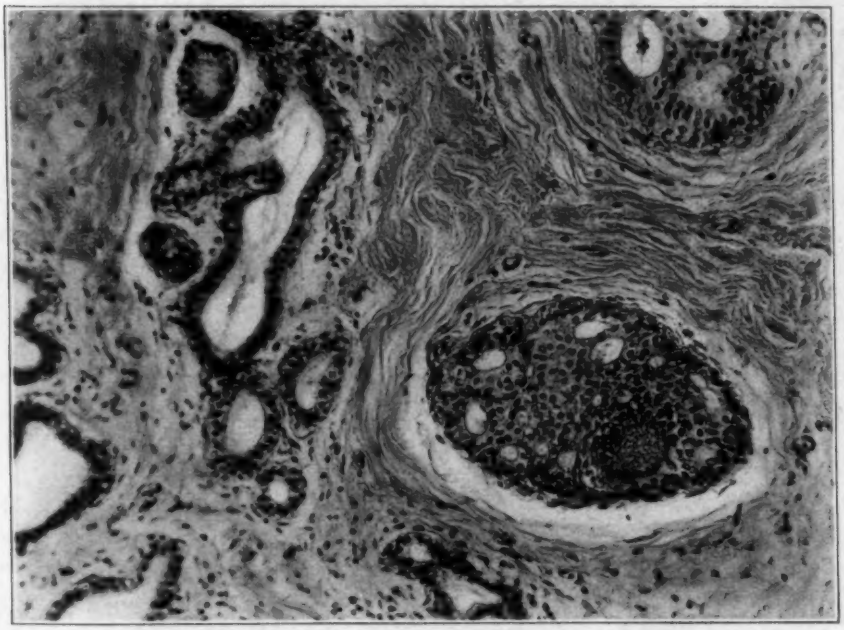

Fig. 9.—Solid epithelial structure with several small lumina.

and were classified with those commonly observed in cystic breasts. Hyperplasia in this definitely not neoplastic condition varies greatly as to its intensity and forms a continuous chain until it assumes the character of an infiltrating malignant growth. There seems to be conclusive evidence that the carcinoma develops from multiple centers within the breast, with gradual transition between the hyperplastic and the carcinomatous foci. We are left in doubt occasionally whether the process should be considered already as carcinomatous or still as hyperplastic. We classify these changes, therefore, as precancerous. It is noteworthy that carcinoma developing in a hyperplastic cystic breast is prone to imitate the structure of its matrix, and the cells of the car-

cinoma differentiate occasionally well enough to simulate those of the hyperplastic breast gland.

The importance of the relationship between carcinoma and the cystic changes was emphasized in our material in several cases (462, 1121, 1406 and 5221) in which we could not demonstrate real infiltrative growths, yet the morphologic appearance of the hyperplastic epithelium was already suggestive of carcinomatous tissue. We considered these as precancerous changes. As a matter of fact they were identical with changes that are readily observed in the vicinity of frank carcinomatous

Fig. 10.—Medullary carcinoma of the breast resembling epithelial proliferation in cystic cirrhosis.

foci. Whether these precancerous changes were about to develop really invasive tendencies remains to be proved, although it seems highly probable.

One of the most contested questions is the importance and frequency of fibrosis in a breast with cystic changes. Extensive fibrosis was present in thirty-two of our own cases, while in four fibrosis was but part of a chronic productive and suppurative process. Fibrosis was of less extent and prevalence in the other cases. These figures show that the coincidence of real inflammatory changes with cystic disease of the breast is rare, which makes their rôle in the pathogenesis of the disease at least questionable. Fibrosis, on the other hand, without evi-

dence of inflammatory changes is so common and is present in so many cases to such an extent that a pathogenic connection between fibrosis and cystic disease seems to be logical.

Fibrosis of noninflammatory origin could be the result of senile atrophy. But the age of our patients does not justify the assumption of senile involution. As a matter of fact, fibrosis of the breast in comparatively young women has been observed by us as well as by others. This would rule out senile involution and would leave only one explanation, that is, development of fibrosis on the basis of regressive changes of the breast gland with substitution of the decaying parenchyma by connective tissue. This conception is borne out by morphologic evidence as well as by physiologic considerations. Regressive changes of the breast gland were easily demonstrable in many of our cases. They include vacuolization due to intracellular hydrops or deposit of fat, and formation of hyalin in the cytoplasm with discharge of hyaline droplets into the lumen. They may result in the breaking up of the impaired cells. Dilatation of the glandular structures on account of retention brings pressure to bear on the lining cells which assume subsequently a more flat shape, so much so, that they resemble endothelial cells.

Breast glands presenting such regressive changes with or without cystic dilatation are usually surrounded by loose connective tissue which invades the lobules and tries to separate the individual glands. The glands are less and less numerous in the advanced stage until most of the lobule is substituted by connective tissue. Yet the outlines of the lobule are still maintained and marked by a ring of dense hyaline connective tissue fibrils. Sometimes part of the lobule is fibrosed and contains but a few discrete glands, while other parts of the same lobule are practically unaltered or show only incipient degenerative changes.

Regressive changes of the breast gland are physiologic, particularly after pregnancy, as involution succeeds the massive hyperplasia of gestation. Similar changes, although much less conspicuous, are observed during the course of menstruation (Loeb,[37] Rosenburg[38]). It is true that the authors are not in accord about the extent and the importance of the menstrual changes of the breast gland. Yet clinical evidence already shows that the breast gland participates in the physiologic changes of the menstrual cycle. On the other hand, it seems that the extent of these changes varies individually.

The morphologic changes of the breast gland which have been described as occurring during menstruation are quite comparable to those observed in fibrosis of the breast gland. The similarity is enhanced by the fact that hyperplastic processes alternate with the regressive

37. Loeb and Hesselberg: J. Exper. Med. **25**:285, 1917.
38. Rosenburg: Frankfurt. Ztschr. f. Path. **37**:466, 1922.

changes. The only, but apparently essential, difference is the formation of interglandular connective tissue with subsequent hyalinization. The onset of regeneration with epithelial hyperplasia is obviously interfered with by the presence of massive connective tissue formed between the glands. Cystic dilatation is most probably also closely connected with the interstitial process, as mechanical dilatation (retraction of shrinking hyaline fibrils) plays a rôle in addition to that played by retention of glandular discharge.

It is illuminating to compare the observations just described, characteristic of mammary fibrosis, with similar changes in other glandular

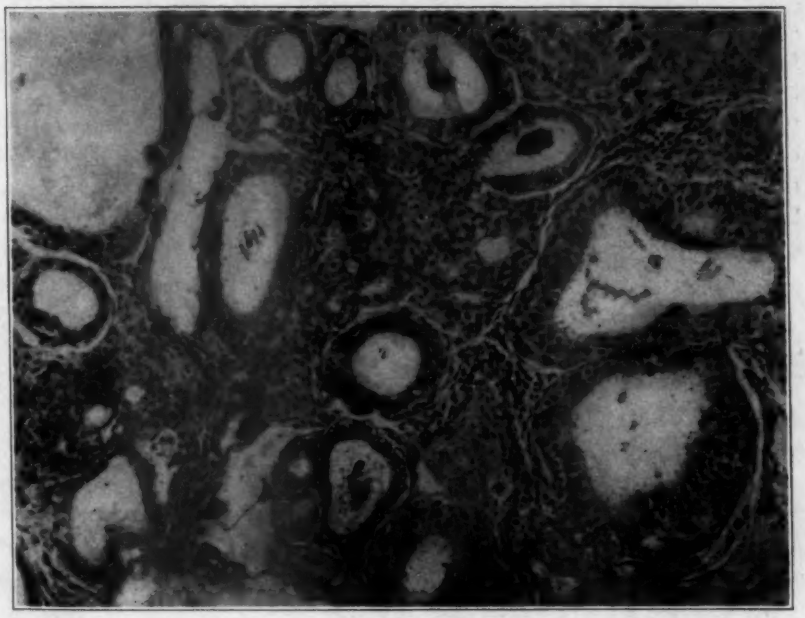

Fig. 11.—Adenocarcinoma of the breast simulating the glandular structures of cystic cirrhosis.

organs such as the liver. Liver cells degenerate and disappear frequently under physiologic conditions. They are easily replaced by proliferation of adjacent cells, or by new formation of liver cells at a distance with readjustment of the architecture. If the disappearing liver cells are not replaced by their own kind, either owing to lack of regenerative power or to the excessive volume of the defect, connective tissue takes up the space of the lost parenchyma. Hyperplasia of the periportal connective tissue is concomitant. Interstitial fibrosis is often followed by more or less substantial hyperplasia of the persisting liver parenchyma which may terminate in the formation of nodules, practically identical with liver cell adenoma.

These changes, if fully developed, constitute the histologic picture of cirrhosis of the liver and justify the following definition of the condition: regressive changes of liver cells, substitution of the lost parenchyma by scar tissue and secondary hyperplasia of the persisting epithelial elements (Kretz). The analogy between the changes constituting cirrhosis of the liver and those characteristic of the cystic disease of the breast is striking. This analogy goes even farther and applies also to the relationship of both conditions to neoplastic processes. The relationship of nodular hyperplasia and adenoma occurring in cirrhosis of the liver to liver cell carcinoma has been dealt with extensively before by one of us.[39] It is generally accepted now that liver cell carcinoma develops in the overwhelming majority of cases from previous hyperplasia which had developed in the course of cirrhosis. When the histogenesis of cirrhosis of the liver is compared with nodular hyperplasia and its occasional transformation into liver cell carcinoma, on the one hand, with fibrosis of the breast, cystic hyperplasia and finally the development of adenocarcinoma on the other, the almost parallel behavior of the two different tissues is striking. It seems, therefore, that the term "cystic cirrhosis of the breast" appropriately describes the real nature of the process and emphasizes that its histogenesis is analogous to similar conditions in other organs. The only difference between cirrhosis in the liver and that in the breast is the cystic character of the lesion in the latter. This, however, is understood without difficulty by comparing the two different matrices, the acinous glands of the breast and the solid trabeculae of the liver parenchyma.

What we propose to call cystic cirrhosis of the breast has been given so many names already by other authors that a new name seems superfluous. Yet most of these names are misleading, being based on erroneous assumptions or misinterpretations; others do not imply the essential characteristics of the condition. Polycystoma, for instance, suggests a neoplastic condition; hydrocystoma and its various modifications, as suggested by Krompecher, are based on the assumption that the lesion develops from aberrant sweat glands; cystic disease of the breast is noncommittal and therefore is a name of little value.

Among the varied features of cystic cirrhosis, the appearance of eosinophil cells has been most puzzling. These cells are also spoken of as "pale cells," probably because when van Gieson's method is used, they stain a faint yellow. The fully developed pale cell resembles the sweat glands of the epithelium. Yet these cells are large and assume peculiar staining properties on account of accumulation of some probably albuminous matter in their cytoplasm which we interpreted as the

39. Goldzieher, M. A.: Virchows Arch. f. path. Anat. **203**:75, 1911.

expression of a metabolic disturbance. The early stage of these changes is readily demonstrable in some of the glands of otherwise unchanged breast tissue. The same is observed occasionally in fibro-adenoma of the breast. We could show also transitions between eosinophil and ordinary epithelium in cysts that were lined partly with fully developed eosinophil cells and partly with ordinary or flat epithelium. Krompecher tried to substantiate the sweat gland nature of the eosinophil epithelium by calling attention to the presence of a layer of spindle-shaped cells which surrounds the eosinophil cysts. He interpreted these cells as smooth muscle elements. He identified them with the muscle cells which are an intrinsic part of the sweat gland structure. However, their interpretation as muscle cells is not convincing. Moreover, we were able to show that some of these cells line capillary spaces which run parallel to the wall of the cyst. Some of these capillaries contain red blood cells, while others are empty and seem to be only lymph spaces. Thus it is fair to classify these cells with endothelium and to reject Krompecher's developmental theory which is based on the mere morphologic resemblance of the pale cells and spindle cells to the constituents of sweat glands. The striking resemblance between these pathologic elements of the diseased breast and those of the sweat glands is elucidated by referring once more to the analogy between cystic cirrhosis of the breast and cirrhosis of the liver. Liver cells, after having undergone regressive changes are prone to assume the appearance of bile duct epithelium. Whole trabeculae of liver cells are transformed occasionally into structures that simulate small bile ducts. This process has been interpreted as a reversion of the liver cells by loss of differentiation to a more primitive cell type. Such pseudobile ducts are prone again to develop progressive changes, and they participate in the formation of both new liver tissue and tubular adenomatous structures.

The occurrence of similar metaplastic changes in the breast gland is well conceivable. The breast gland cell may also lose its differentiation and revert thereby to a more primitive type which is the common matrix of both breast and sweat gland cells. If differentiation sets in again, the newly produced tissue may easily assume the sweat gland type. Similar indirect metaplasia is known to occur in other glandular organs or on mucous membranes. The assumption of indirect metaplasia seems to us a much more likely explanation of the sweat gland-like structures in the breast than the hypothetic misplacement or malformation of sweat glands. Yet we also believe that it is not necessary to fall back on the assumption of indirect metaplasia, as metabolic disturbances of the breast gland cells account for changes that are morphologically identical.

CONCLUSIONS

1. Forty-seven cases in which breast glands were removed surgically were studied.

2. The development of cysts in the breast was presented as a primary degenerative lesion associated with perilobular and intralobular fibrosis and completed by hyperplastic changes of the epithelium.

3. "Cystic cirrhosis of the breast" is suggested as a more adequate terminology.

4. The development of eosinophil epithelium is interpreted as a metabolic disturbance of the breast gland cells, which thereby simulate the appearance of sweat gland epithelium. The process is suggestive of indirect metaplasia and does not warrant the assumption of developmental errors.

5. Hyperplastic changes of the epithelium frequently assume the character of precancerous lesions.

6. The frequent coincidence of cystic cirrhosis, precancerous changes and carcinoma emphasizes the importance of cystic cirrhosis in the pathogenesis of carcinoma of the breast.

7. The histogenesis of cystic cirrhosis of the breast is analogous to cirrhosis of the liver. The analogy is enhanced by the frequency with which adenomatous and carcinomatous neoplasia develops from the originally hyperplastic condition.

CARCINOMA OF THE LARGE BOWEL NOT INCLUDING THE RECTUM AND THE RECTOSIGMOID

CHOICE OF OPERATIVE PROCEDURE *

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Operation for radical cure of carcinoma of the large bowel is a hazardous procedure. The early mortality was high but has been lowered slowly by the development of the stage operations as well as by proper preoperative preparation and postoperative care. Further decrease in operative mortality and increase in postoperative longevity can be accomplished by standardization of operative procedures. This can be accomplished only when the factors relative to death following operation and to the recurrence of carcinoma are generally known. The factors vary with the locations of the lesions in the large bowel.

GENERAL CHARACTERISTICS

Incidence.—It is interesting to note the incidence of carcinoma of the large bowel compared to that of other parts of the body. By statistics this is shown to be increasing. In a series of nearly 70,000 autopsies, Nothnagel, Azerman, Muehler and Madyl found 5,796 deaths from carcinoma. One fourth of the cancers causing death were located in the intestinal canal: 35 were in the cecum; 83 in the sigmoid; 131 in other parts of the colon, and 262 in the rectum. The colon is the site of more cancers than any other portion of the alimentary tract, with the exception of the stomach.

The frequency of occurrence of carcinoma in the several portions of the colon is shown by Judd in a report of 333 cases. In a report of 333 cancers of the colon, he gives the location as follows: cecum and ascending colon, 159 (47.4 per cent); hepatic flexure, 29 (8.7 per cent); descending colon, 75 (22.5 per cent). He also reported 292 cases occurring in the sigmoid flexure. This series closely corresponds to the series of Erdmann and Lockhart-Mummery.

The statistics of Crumpson and Canderceer, Clood, Debocis and the Mayo Clinic show that males are afflicted in a proportion of approximately two to one.

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* From the Department of Surgery, Woodland Clinic.
* Read at the Idaho State Medical Meeting, July 7, 1929.

Occurrence in Decades of Life.—Carcinoma of the large bowel may occur at any age, and, although it is usually found in the fifth and sixth decades, it is not unusual to find it in the second decade, and numerous cases are reported in which the patients were between 20 and 30 years of age. Cases have been reported in which the patients were 3, 5, 14 and 15 years of age.

Pathology.—The anatomic types of carcinoma of the colon are: (1) the soft medullary adenocarcinoma, (2) the scirrhotic or fibrosarcoma and (3) the colloid. The different pathologic types are responsible for the wide variations in the symptoms as well as in the roentgenologic observations. Cancers of the right half of the colon, as a rule, are large and irregular and are covered with stubby protuberances. They frequently ulcerate and often produce large masses. In a study of the mortality and recurrence in 203 patients with colloid carcinoma of the gastro-intestinal tract, Parham found a greater longevity, but a greater eventual mortality. Obstruction is not common, except by reason of adhesions of secondary intussusception. In the colloid type the epithelium frequently forms glands, the lumina of which may be greatly distended by secretion. The glandular type is the least rapidly fatal, owing to the tendency of the secretion to interfere with the nutrition of the cancer cells.

The scirrhotic type is chiefly composed of adenocarcinomatous islands surrounded by dense connective tissue. The tumor mass is usually small and annular. Obstruction is, as a rule, an early symptom. The usual site of the tumor is in the left quadrant.

Cancers vary greatly in their degree of malignancy, as was pointed out by Broders in his index of the grading of malignancy. The degree of malignancy is based on the differentiation of the neoplastic cell. The more nearly the cell approaches the embryonic, or undifferentiated, type, the more malignant the tumor. The converse is true; namely, that the more nearly normal the tumor cell is, the lower is the degree of malignancy.

The extension of malignancy from the primary growth is by way of the lymphatics or the blood stream, by cellular implants on the mucous membrane or the serosa of the wall of the bowel and by direct extension.

Jamison and Dobson divided the lymphatics into four groups: (1) the epicolic group commencing with the surface of the bowel (fig. 1); (2) the paracolic group in the mesocolon, close to the bowel (fig. 1); (3) the intermediate group along the colic arteries (fig. 1), and (4) the main glands at the origin of the main artery (fig. 2).

The lymphatics, as a rule, follow well defined lines, usually accompanying the blood vessels of the part (fig. 1). The lymphatic supply of the cecum and ascending colon is extensive when compared to the rest of the colon. It seems to act as a defensive mechanism since metastases occur more slowly there than in any other portion of the large

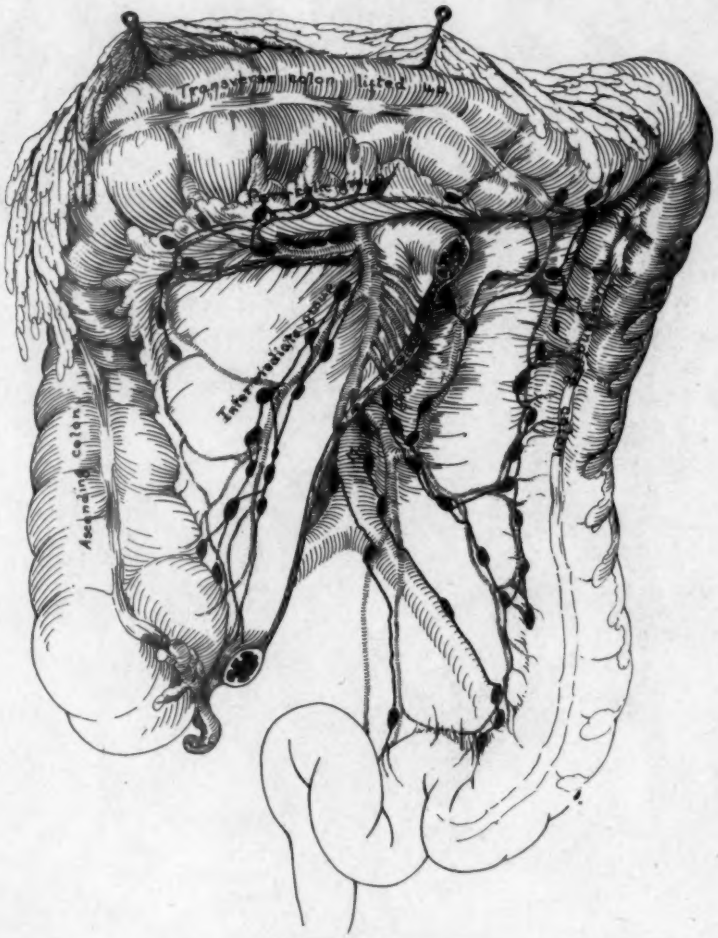

Fig. 1.—Lymphatics of large bowel.

bowel. The lymphatic supply of the descending portion of the large bowel is the least of any of the segments.

In a study of 100 specimens of colonic cancer, Hayes observed metastases in the order of frequency to occur in the sigmoid, descending colon, transverse colon, hepatic flexure, splenic flexure and ascending colon. Early metastasis to the liver without appreciable local glandular

involvement is usually an accidental involvement by way of the larger venous tracts. Cancer cells that break off are carried directly to the liver at an early stage of the disease.

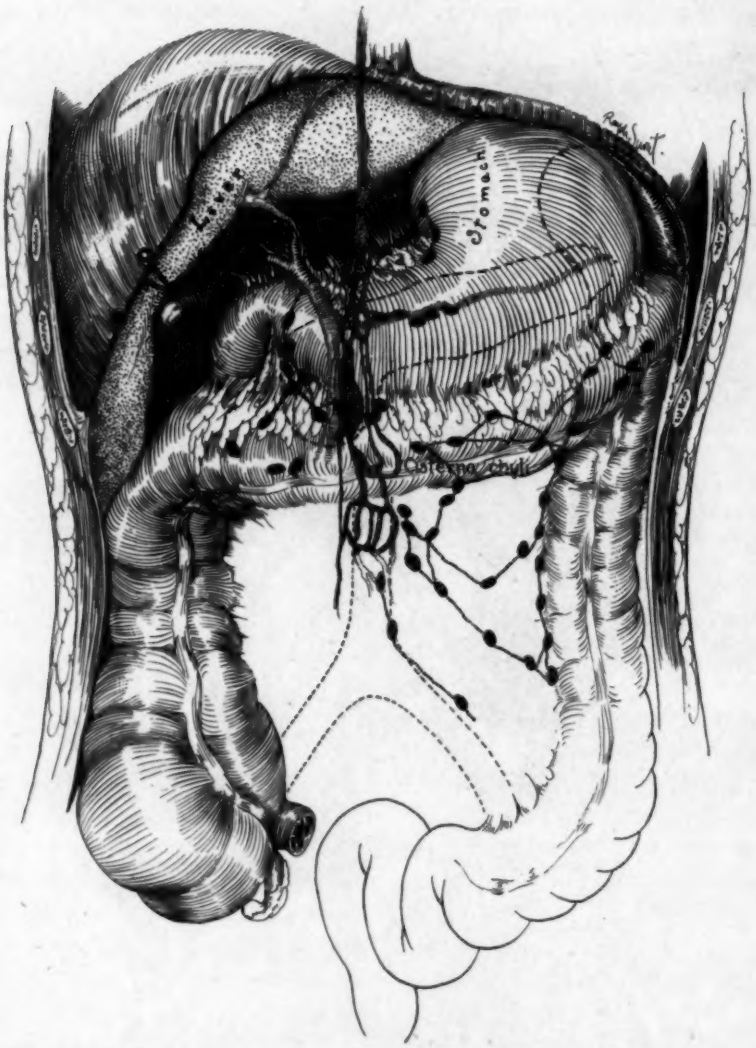

Fig. 2.—Relationship of lymphatic drainage to cisterna chyli and portal circulation.

Metastatic implants on the inside of the bowel usually occur by back pressure and peristalsis. Masses of carcinoma cells which have been broken off the original tumor are often implanted several inches away from the primary growth.

Carcinoma cells, breaking off from the serous surface, may likewise find lodgment at distant parts of the abdomen, by gravity, often low in the pelvis.

Location of Lesion.—Roentgenologists are agreed that the barium sulphate enema is the most efficacious method for exact localization of

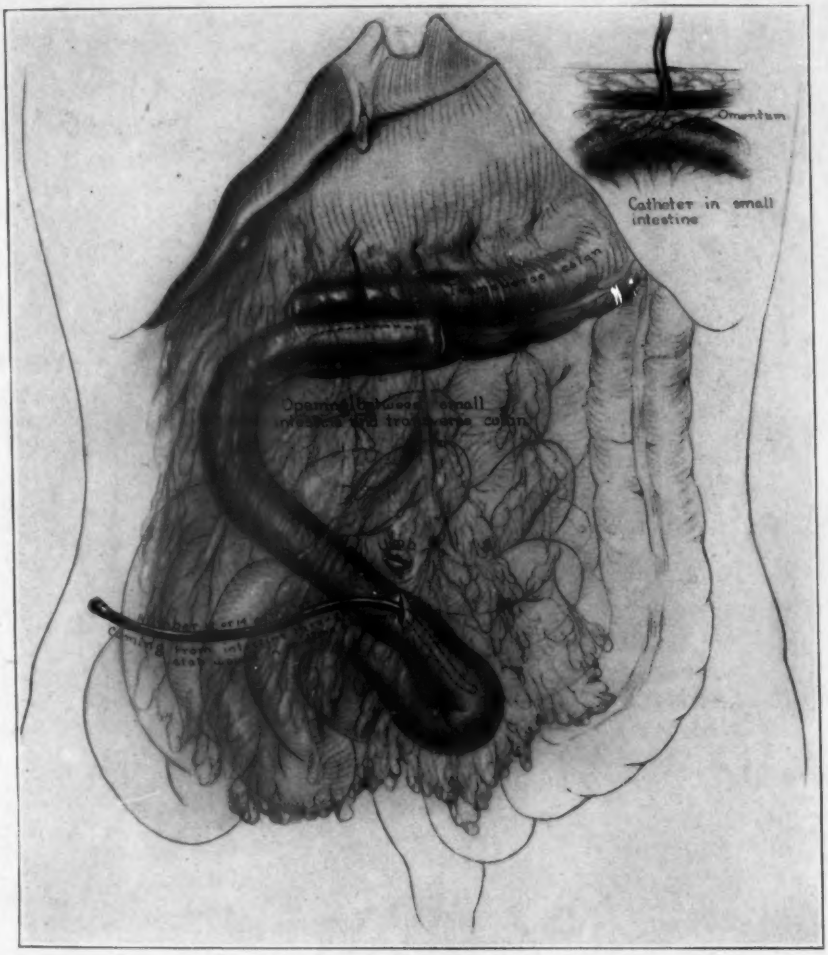

Fig. 3.—Plan of resection involving right half of colon.

the carcinomatous lesion. It is inadvisable to give barium by mouth if obstructive symptoms have been at all marked, owing to the impaction of this material above the lesion. Unfortunately, obstruction is the first symptom noted. The patient so afflicted may become markedly debilitated before surgical measures are instituted. In this instance

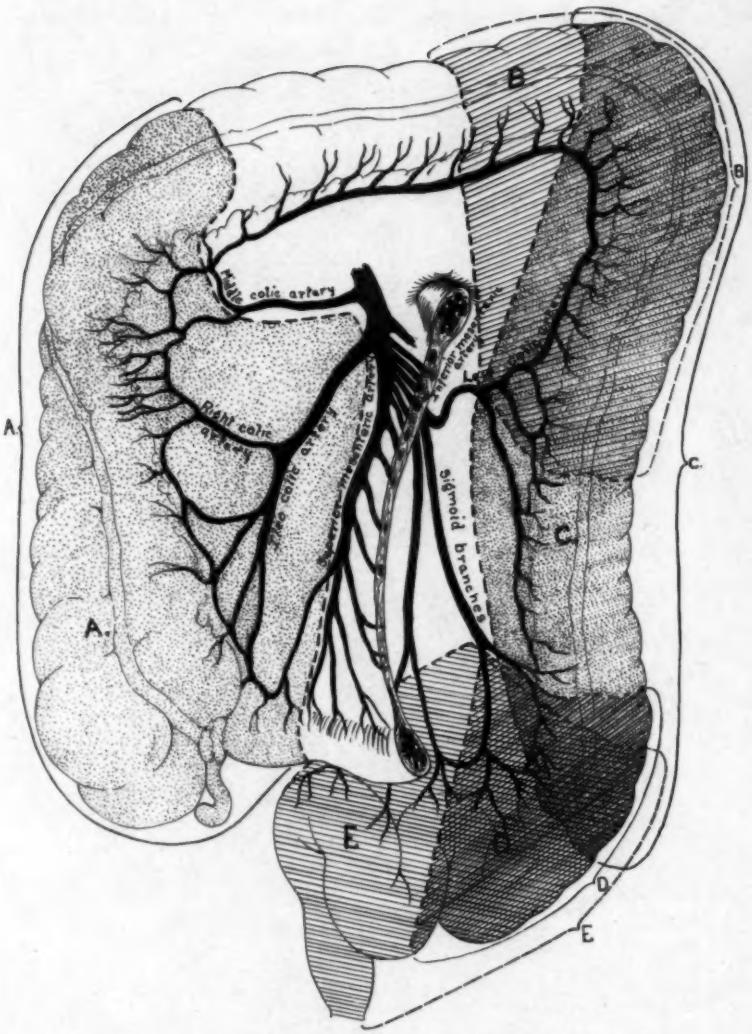

Fig. 4.—Defined areas of resection according to blood supply of large bowel. *A* indicates area of bowel to be resected in carcinoma of cecum, ascending colon and hepatic flexor, the area between *A-B* to be resected for carcinoma of the transverse colon to save, if possible, the middle colic artery; *B*, area to be resected for carcinoma of the splenic flexor of colon; *C*, area to be resected in ascending colon if extensive glandular metastasis exists; *D*, area which may be resected if small early carcinoma of the sigmoid exists, and *E*, usual area for abdominal perineal resection of the sigmoid and rectum.

extensive examination should not be done, and cecostomy or ileostomy under local or regional anesthesia, without exploration, is the procedure of choice.

OPERATION

Preoperative Preparation.—The initial efforts should be directed toward the correction of obstruction if it exists and toward the restoration of body fluids.

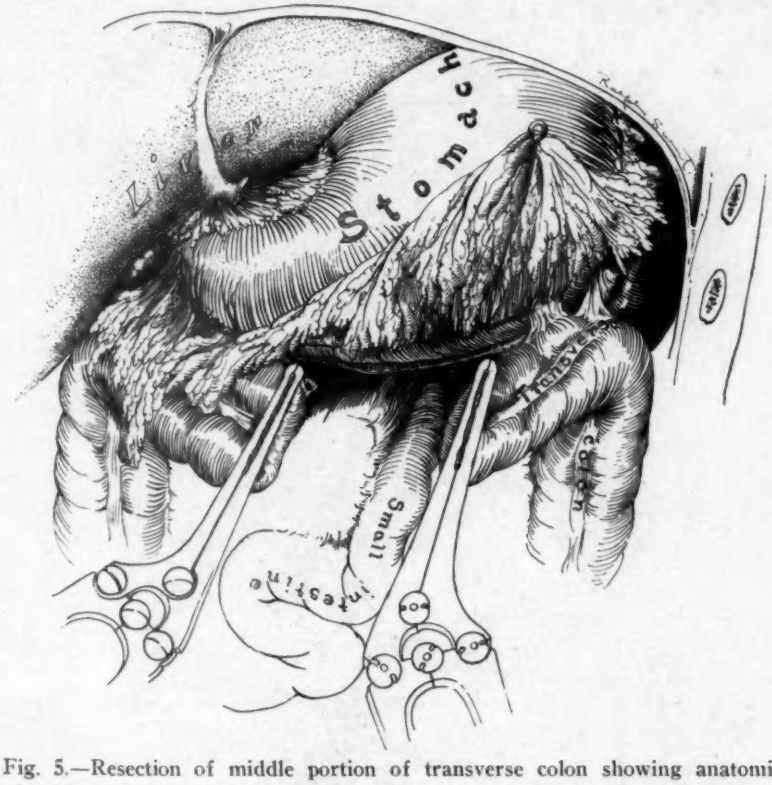

Fig. 5.—Resection of middle portion of transverse colon showing anatomic relationship and ends ready for choice of anastomosis.

Marked anemia exists in many instances, associated with lesions in the right quadrant. Repeated transfusions may be necessary. Chronic myocarditis, chronic nephritis and hypertension are not unusual complications. Prolonged obstruction with resulting toxemia may greatly damage an already defective cardiorenal mechanism. Examination of the blood urea and nonprotein nitrogen and phenolphthalein tests should be made to ascertain how the kidney is functioning. Before an operation of such magnitude as resection of the bowel is considered, electrocardiographic studies of the heart should be made if myocardial damage

exists. Operability can be determined only by careful abdominal exploration after the lesion has been localized by barium enemas. However, exploration of the abdomen should not be done without careful preparation when any appreciable degree of obstruction exists; nor is prolonged exploration well tolerated when debility is marked.

Fig. 6.—Parker-Kerr closed technic of resection of transverse colon.

Surgeons are universally agreed that operation by well defined stages should be instituted in the presence of obstruction. Cecostomy or ileostomy through a small incision, under local anesthesia, is then the procedure of choice in preparation.

Postoperative herniations and extensive wound infections are common complications when an ileostomy or cecostomy is done through the incision for exploration.

Lesions that are immobile before drainage of the bowel may become mobile in from two to three weeks, owing to the subsidence of inflammatory reactions.

Choice of Procedure.—In planning an operation for radical cure of carcinoma of the bowel, it is necessary to have clearly in mind both the immediate and the ultimate causes of death, as previously pointed out. Before the advent of the two-stage operation for prostatectomy, the postoperative mortality was very high. The mortality was primarily caused by urinary obstruction and was secondary to infection. So it is with obstructive lesions in the large bowel, with infection playing an even more important rôle. Infection at the time of operation is usually easily overcome by the patient if average aseptic technic has been

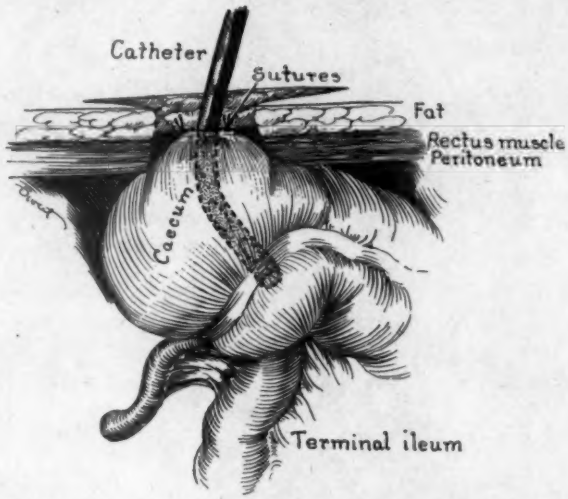

Fig. 7.—Technic of cecostomy through as small an opening as possible.

observed. The large percentage of immediate death occurs from one of the following causes: (1) the resulting paresis and obstruction of the bowel at the operative site from gas pressure; (2) improper selection of the area of resection and the resulting gangrene of the bowel from lack of blood supply, with resulting peritonitis; (3) infection and abscess formation in the wall of the bowel at the site of the suture line, if extensive fat deposits exist, and (4) institution of radical operative procedure before sufficient preoperative preparation has been accomplished.

The less common causes of immediate death are: (1) pneumonia, if ether anesthesia or prolonged gas anesthesia is used; (2) postoperative shock from prolonged operative procedure or hemorrhage; (3) pulmonary embolus, and (4) thrombosis of vessels when tumors have been dealt with by the Mikulicz and Paul methods.

The ultimate cause of death is from recurrence of the carcinoma. Recurrence can be minimized if radical resection is instituted in the

cases considered operable. Consideration of lymphatic and blood supply of the large bowel cannot be overemphasized in considering the segment of bowel to be resected.

Carcinoma of the cecum, ascending colon and hepatic flexure usually is not markedly obstructive. If obstruction does not exist, a primary

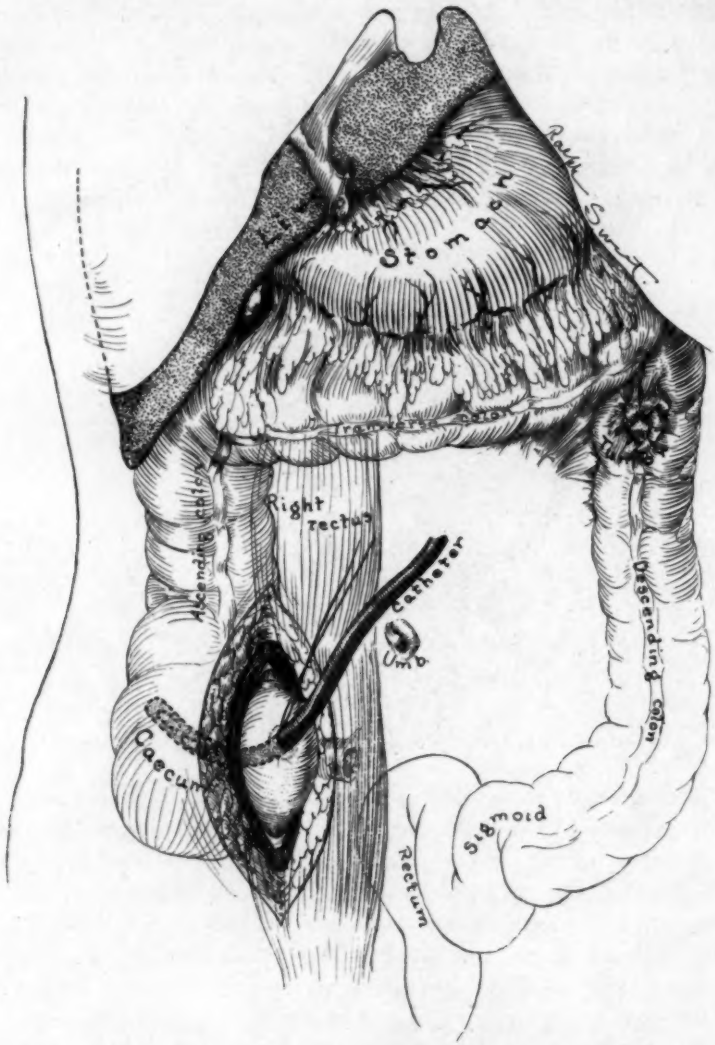

Fig. 8.—Position of cecostomy in relationship to tumor mass.

resection can usually be done (fig. 3). This operative procedure is unquestionably the safest when the factors of blood supply (fig. 4) and lymphatic supply (figs. 1 and 2) are considered. The extent of the resection is shown as *A* in figure 4. Supplementary ileostomy is

advisable at a point removed from the incision if obstruction exists to any considerable degree at the time of primary resection.

Carcinoma arising in the transverse colon can be dealt with by a primary resection (figs. 5 and 6). Cecostomy (fig. 7) or ileostomy is advisable if the patient is old or the obstruction is appreciable. Partial

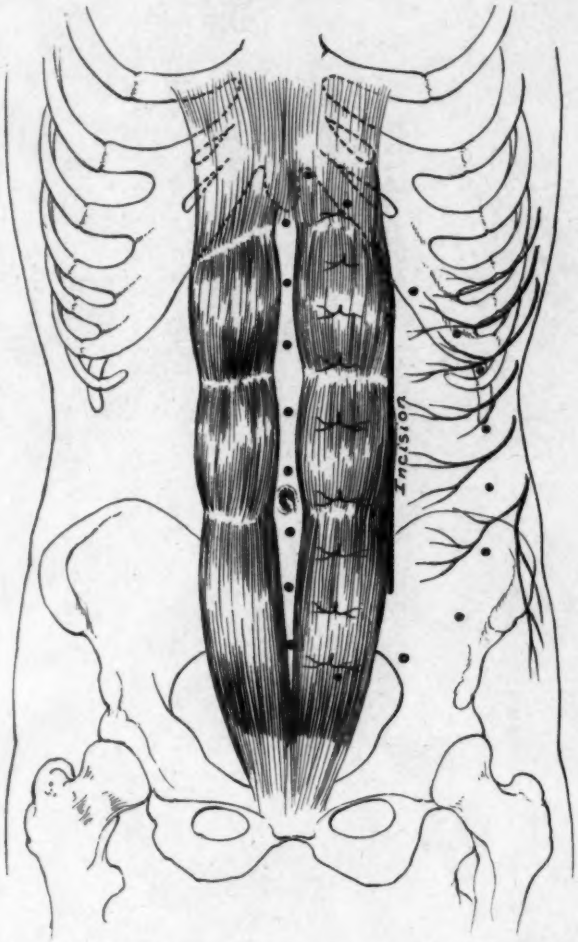

Fig. 9.—Areas of infiltration of the abdominal wall for exploration and resection of tumor of colon under anesthesia.

obstruction that is not greatly improved by medical management should have a preliminary cecostomy done.

Due to the extensive mobilization of the splenic flexure, lateral anastomosis, supplemented by a preliminary cecostomy, is, as a rule, the operation of choice.

Carcinoma of the splenic flexure usually produces obstruction, which is the outstanding symptom. The blood supply is poor (fig. 4 *B*).

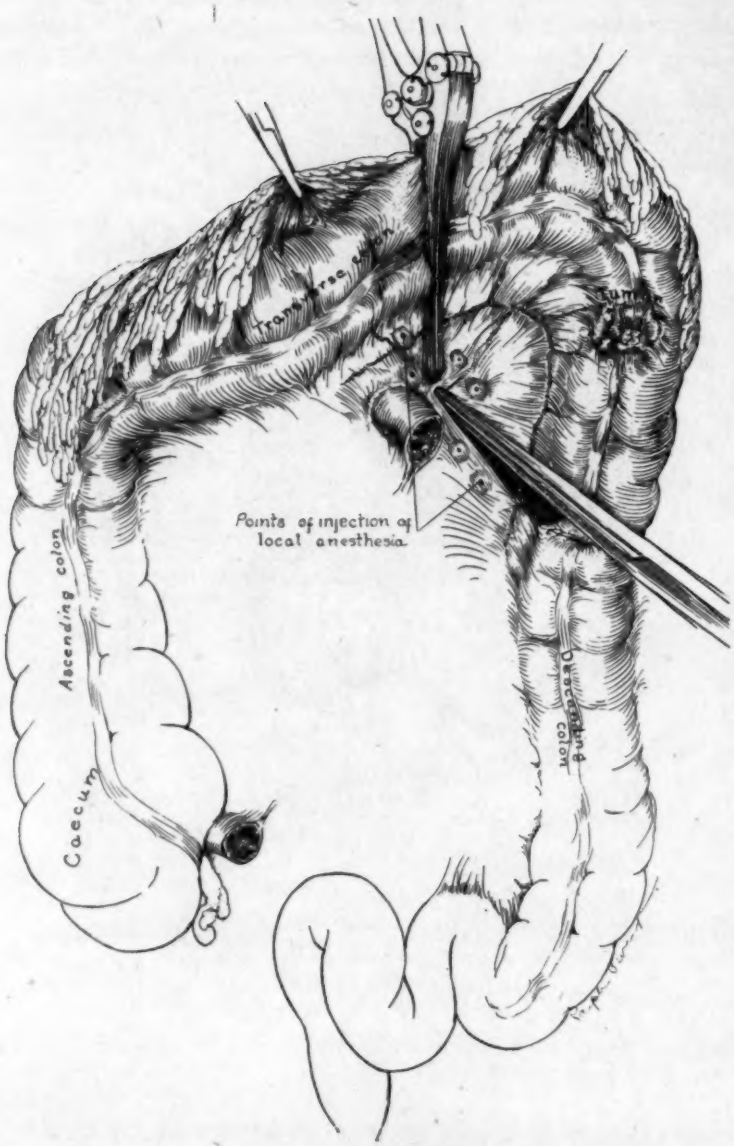

Fig. 10.—Resection of bowel segment by local infiltration of the mesentery.

Preliminary cecostomy (figs. 7 and 8) followed by radical resection (figs. 10 and 11) under regional anesthesia or spinal anesthesia, supplemented by light ethylene (fig. 9), is the procedure of choice.

In the descending and sigmoid colon a preliminary cecostomy should be done in all cases in which obstruction is marked. Radical resection

Fig. 11.—Lateral anastomosis of the transverse colon and decending colon following resection. Mobilization accomplished by splitting leaf of outer mesentery.

according to the closed technic as outlined in figure 6 is the preferable technic. Resection should be wide, as in *C* in figure 4, if glandular involvement is present.

As far as possible local, regional, spinal or ethylene anesthesia should be used.

COMMENT

Nine cases of carcinoma of the colon, not including the rectum and sigmoid, have been selected for analysis as to the choice of operative procedure influencing the immediate and ultimate mortality. In a previous article I reviewed a group of cases of carcinoma of the rectum and sigmoid from a similar point of view.

The three Mr. B.'s are three of six brothers who have had resections of the cecum and ascending colon for carcinoma of the cecum.

Analysis of Nine Cases

Cases	Age	Type of Operation	Date of Operation	Location of Lesion	Grade of Malignancy	Results	Living	Type of Carcinoma
Mrs. W.	74	Cecostomy resection lateral anastomosis	1/ 5/27 2/ 5/27	Splenic flexure	II	Good	2 years	Adenocarcinoma
Mrs. L.	30	Resection lateral anastomosis	4/ 7/25	Transverse colon	IV	Good	4 years	Adenocarcinoma
Mrs. H.	58	Ileostomy	9/30/27	Cecum (marked obst.)	?	Died 24 hours	Died	?
Mr. B.	37	Resection cecum	9/12/27	Cecum	III-plus	Good	1½ years	Adenocarcinoma
Mr. M.	43	Resection transverse colon and cholecystotomy	5/17/28	Transverse colon (marked obst.)	III	Died 3 days	Died	Colloid carcinoma
Mr. F.	77	Cecostomy resection lateral anastomosis	5/14/27 5/23/27	Upper descending colon	III	Good	2 years	Adenocarcinoma
Mr. T.	40	Resection transverse colon	5/12/24	Transverse colon with involvement duodenum	III	Died 1/19/25 recurrence in liver	Died	Adenocarcinoma
Mr. B.	52	Resection cecum and hepatic flexure	5/27/28	Cecum	IV	Good	2 weeks	Adenocarcinoma
Mr. B.	43	Resection cecum abdominoperineal	6/20/22 8/29/29	Cecum Rectosigmoid	III II	Good Good	7 years 1 year	Adenocarcinoma Adenocarcinoma

Patient 9 developed a carcinoma of the rectum seven years after the resection of the cecum and has had an abdominoperineal operation for radical cure. Another brother has a marked diverticulitis of the cecum and sigmoid at the present time.

This family group illustrates the marked inherited susceptibility to the development of carcinoma. The instability of the patient's tissue for further development of carcinoma is illustrated in patient 9, who developed the rectal neoplasm seven years later. An additional case is cited from the records of a woman who had a grade III carcinoma of the breast removed and who two years later developed a carcinoma of the rectum.

Mrs. W. and Mr. F. illustrate the old, debilitated, obstructed groups, who require cecostomy and lengthy preparation for resection, the resection being done in these cases entirely under regional anesthesia.

Postoperative irradiation in all cases of cancer of the large bowel and rectum is considered an essential routine in the prevention of recurrence. It is felt that the good results obtained in the prolongation of life in the cases in which the patients had a grade III and IV carcinoma is due in a measure to deep therapy.

SUMMARY

The most important principles to be stressed are: 1. Relief from obstruction and cleansing of the bowel preoperatively and postoperatively should be done for relief from toxemia. Old and debilitated patients have poor healing powers. Gaseous distention from partial ileus and local peritonitis separates poorly healed suture lines in numerous cases. The safest procedure as a routine is that of a supplementary ileostomy when primary resection of the cecum, hepatic flexure or transverse colon has been done, if obstruction exists. Preliminary cecostomy or ileostomy at the time of radical resection, or previously, should be instituted when dealing with carcinoma of the splenic, descending or sigmoid colon, depending on the degree of obstruction and debility. It is possible to do primary resections of the large bowel when the patient is in good physical condition and mildly obstructed without ileostomy or cecostomy if sufficient bowel cleansing preparation has been previously instituted and obstruction relieved. Preliminary preparation with excess of fluids and nonresidue diet should be followed as a routine.

2. Careful attention to the blood supply of the bowel stumps before anastomosis is begun will avoid subsequent sloughing from lack of blood supply. If possible, resections should be planned according to the blood supply shown in figure 4, with the lymphatic supply illustrated in figures 1 and 2, in mind. The anastomosed segments should be mobilized so that all tension is avoided.

3. Preoperative preparation in regard to the restoration of water balance, medical therapy directed to the improvement of impaired kidneys and damaged cardiovascular system, correction of anemia and inanition are factors of vital importance for a successful outcome of a radical surgical procedure.

4. The operation of Mikulicz should be abandoned owing to the length of hospitalization, high percentage of recurrence, danger of thrombosis in vessels and postoperative herniation. The operative risk is not greater than that of a cecostomy followed by radical resection. It should be used only as an emergency procedure in case of gangrene of the bowel at the time of the primary operation.

5. Postoperative deep therapy should be done as a routine.

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HYPERTONICITY WITH HYPERTROPHY OF THE PYLORUS IN ADULTS

SURGICAL ASPECTS *

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It is my purpose to call attention to a syndrome that seems to constitute a definite clinical entity, but one that the clinician seldom if ever takes into consideration when confronted with a patient who complains of discomfort in the upper part of the abdomen. It was brought to my attention by three patients who were seen recently at the University of Virginia Hospital. In each instance roentgenologic studies of the gastro-intestinal tract were made, and in all of them rather characteristic changes in the pylorus were noted. The roentgenologic observations will be reported in detail elsewhere by Archer.[1] Exploration of the abdomen revealed almost identical changes in each case; namely, hypertonicity and hypertrophy of the pylorus with narrowing of its lumen.

REPORT OF CASES

CASE 1.—C. D., a white man, aged 63, was admitted to the medical service on Jan. 5, 1926. Except for the fact that his father died of "cancer of the liver," the family and past histories were unimportant. The chief complaint was soreness in the upper part of the abdomen, which had first been noticed five months previously. There had been little real pain, but the discomfort had been constant and accompanied by the sensation of a "lump" in the epigastrium. There had been no apparent relationship between the discomfort and the taking of food. Nothing had relieved the symptoms. Nausea and vomiting had occurred on several occasions, but there had been no hematemesis and no melena. The patient had lost 25 pounds (11.3 Kg.).

Examination revealed the patient to be somewhat undernourished. All of his teeth had been extracted. The heart and lungs were normal. There was some tenderness and rigidity of the upper portion of the rectus muscle on the right side, but no mass was palpable. The temperature, pulse rate and respirations were normal. The urine and blood did not show any abnormality, and the Wassermann reaction was negative. The systolic blood pressure was 126 and the diastolic 78. Analysis of 90 cc. of brownish material withdrawn from the stomach showed no free hydrochloric acid, but blood, lactic acid and bacilli Oppler-Boas were present. A roentgenologic study of the stomach revealed a constant but regular narrowing of the pyloric ring that appeared to be about an inch in width.

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* From the Department of Surgery and Gynecology, University of Virginia.

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It was thought that the patient had an early and operable case of gastric carcinoma, and operation was advised.

Operation was performed under ether anesthesia by Dr. S. H. Watts. A rather elastic mass about 3 cm. in diameter was found in the region of the pylorus. The mass consisted of a greatly hypertrophied pyloric ring, the muscle of which was quite spastic. The stomach, duodenum, gallbladder, pancreas and appendix were normal. The pylorus was incised longitudinally, and closed transversely in order to increase the size of its lumen. Postoperative convalescence was uneventful. A letter received from the patient's physician, March 10, 1929, more than three years after the operation, stated that he was in good health, free from discomfort and had regained his normal weight soon after returning home.

CASE 2.—C. T., a colored man, aged 42, was admitted to the surgical service on March 19, 1928. His family history was unimportant. He had been operated on at this hospital, in 1916, for hemorrhoids, and again in 1922, for chronic appendicitis. At that time the observations made on roentgenologic examination of the stomach were identical with those to be described. The operator reported that there was no palpable abnormality of the stomach at that time. The appendectomy had relieved the symptoms for only a few months.

The chief complaint was soreness and discomfort in the upper part of the abdomen of six months' duration. There had been continuous soreness in the epigastrium, but no real pain. Vague generalized abdominal discomfort had been noticed intermittently for a period of six years. There had seemed to be no constant relationship between the soreness and the ingestion of food. There had been no nausea or vomiting, no hematemesis and no melena. The patient had suffered with moderate constipation since 1922, before the appendectomy.

He was well nourished, and his teeth seemed to be in fairly good condition. The heart and lungs were normal, but the abdomen was moderately tender and somewhat resistant in its upper portion, particularly on the right side. The temperature, pulse rate, respirations and blood pressure were normal. Examination of the urine and blood did not reveal any abnormalities, and the Wassermann reaction was negative. Gastric analysis showed hyperacidity of a moderate degree. Roentgenologic examination of the stomach revealed a tubelike, spastic pylorus with constant spasm of the prepyloric portion of the stomach. The probable presence of a small gastric ulcer was reported.

I performed the operation under ether anesthesia, and exploration revealed a normal gallbladder, stomach and duodenum. The appendix had been removed, and there were no adhesions in the region. To make sure that no gastric or duodenal ulcer had been overlooked the stomach was incised, and the gastric and duodenal mucosa were inspected. The only positive observation was a definitely thickened and spastic pylorus which was not seen to relax at any time, and which offered considerable resistance to digital dilation. No further operative procedure was done.

Postoperative convalescence was uneventful, and the patient left the hospital after two weeks. He returned on November 19, and stated that following operation he had been entirely free from discomfort for four or five months, but that later the discomfort had gradually returned. Cholecystographic examination did not reveal any evidence of cholecystic abnormality, and a roentgenologic study of the stomach did not show any change in the pylorus since the former examination. Small frequent meals were prescribed, and apparently have relieved the patient for the present.

CASE 3.—A. L. J., an unmarried white woman, aged 39, was admitted to the medical service on April 17, 1928. The family history was unimportant. The

uterus had been suspended fifteen years before. The patient had never been able to eat large meals, because her stomach had seemed to fill quickly. Her chief complaint was of periodic attacks of pain in the epigastrium, which had troubled her for fifteen months. The pain had occurred soon after the ingestion of a meal. Sodium bicarbonate had afforded relief, and sometimes there had been relief after the ingestion of more food. Three weeks prior to the time of admission, the symptoms had become more severe and had frequently been accompanied by attacks of vomiting. At the time of examination, the patient had been unable to retain any food for a period of six days. There had been no hematemesis or melena. She had lost 30 pounds (13.6 Kg.).

At examination the patient appeared undernourished, quite intelligent and cooperative. There was some dental caries present. The heart and lungs were normal. There was tenderness and some muscle spasm in the epigastrium, and the upper right quadrant of the abdomen. The temperature, the pulse rate, respirations and blood pressure were normal. Examination of the urine, blood, stools and gastric contents did not reveal any abnormality. Roentgenologic examination of the stomach revealed a tubelike and spastic pylorus with a constant deformity of the lesser curvature just proximal to the pylorus. Six hours later, there was a residuum in the stomach estimated at 25 per cent. Gastric ulcer with pyloric obstruction was suspected, and, after dehydration had been combated by fluids given intravenously, operation was advised.

At operation, a spastic and definitely thickened pylorus was discovered. The stomach, duodenum, gallbladder and appendix seemed normal. The anterior two thirds of the pyloric ring and some of the contiguous stomach and duodenum were excised. Inspection of the stomach and duodenum did not reveal any evidence of ulceration. The opening was closed transversely, a funnel-shaped communication between the stomach and duodenum being left. Examination of the excised tissue showed some hypertrophy, cellular infiltration and edema of the muscularis.

The postoperative course was entirely uneventful, and the patient was discharged after two weeks. Later some diseased teeth were removed. When seen six months after operation, the patient reported a gain of 30 pounds (13.6 Kg.). She was seen again after an additional period of six months, and at that time reported that her health was excellent and that she was entirely free from abdominal complaint.

LITERATURE

Because the condition encountered in these patients seemed uncommon, I examined several textbooks and other literature dealing with gastro-intestinal disease, but I found relatively few and rather unsatisfactory references to dysfunctions of the pylorus in adults. Hypertrophic pyloric stenosis of congenital occurrence in infants was discussed frequently. Numerous data of anatomic and physiologic studies of the pylorus were found.

The anatomic location and structure of the pylorus are such that it plays an important rôle in the digestive processes of the stomach and upper part of the intestinal tract. It is a sphincter-like ring of circularly arranged muscle fibers at the outlet of the stomach. By the reconstruction and study of serial sections, Horton [2] showed that there

2. Horton, B. T.: Pyloric Musculature with Special Reference to Pyloric Block, Am. J. Anat. **41**:141, 1928.

is a sharp break in the circular fibers of the pylorus when it reaches the duodenum, but that there is continuity of about one fourth of the longitudinal fibers from pars pylorica to duodenum, by which the dilator muscle of the pylorus is formed.

The mechanism by which the pylorus opens and closes has not been fully explained. The theory of complete control by acid and alkali has been found inadequate. In regard to nervous control, McCrea and Brandt [3] have shown that the pylorus and duodenum get their nerve supply from a large branch of the vagus leading directly from the region of the cardia to the liver. That nerve fibers from both the sympathetic and the parasympathetic systems supply the pylorus is certain, but which is constrictor and which inhibitory is not agreed on by investigators. Martin and Burden [4] reviewed recent experimental data on the subject.

Pyloric stenosis may be secondary to a condition such as peptic ulcer or gastric carcinoma, or it may be primary. Primary stenosis may be caused by dysfunctions or by changes in the musculature or by a combination of the two. Luminal narrowing of the pylorus due solely to dysfunction was called "pyloric achalasia" by Hurst,[5] who used the term to denote persistent failure of a sphincter to open widely in response to that coordinating mechanism by which visceral contents are alternately retained and expelled. Martin and Burden,[4] and Deaver and Burden [6] in recent studies of such cases described a rational surgical treatment.

Stenosis of the pylorus due solely to changes in the musculature, such as fibrosis and hypertrophy, probably is rare. Stenosis due to a combination of functional and structural causes seems to be the most probable type. Hypertrophic pyloric stenosis of congenital occurrence in infants is a common variety. The first description of this condition is attributed by Osler to Beardsley [7] (1788). Hirschsprung's [8] publication (1887) again directed attention to this condition. Downes [9] is responsible for comprehensive later studies of the surgical problem.

3. McCrea and Brandt, quoted by Mayo, C. H.: Division of the Vagi for Pylorospasm, Proc. Staff Meet. Mayo Clin. **3**:177, 1928.

4. Martin, E., and Burden, V. G.: Pyloric Achalasia and Peptic Ulcer, Ann. Surg. **88**:565, 1928.

5. Hurst, A. F.: The Sphincters of the Alimentary Canal and Their Clinical Significance, Brit. M. J. **1**:145, 1925.

6. Deaver, J. B., and Burden, V. G.: The Surgery of Pylorospasm, Ann. Surg. **90**:530, 1929.

7. Beardsley, Hezekiah, quoted by Osler, William; and McCrea, Thomas: The Principles and Practice of Medicine, New York, D. Appleton Company, 1919.

8. Hirschsprung, quoted by Osler.

9. Downes, W. A.: The Operative Treatment of Pyloric Obstruction in Infants, Surg. Gynec. Obst. **22**:251, 1916.

An interesting conception of the pyloric tumor in such cases was mentioned recently by Freeman.[10] He suggested that it may represent a reversion to ancestral type. In support of his hypothesis, he stated that the gizzard of graminivorous birds is situated in the pyloric region, and that in some higher mammals, notably the colored anteater, the outlet of the stomach is occupied by a heavy muscular tumor in the same situation as the tumor found in cases with hypertrophic pyloric stenosis.

That primary stenosis of the pylorus with hypertrophy might occur in adults seems to have been recognized first by Maier.[11] He reported necropsies of twenty-one subjects varying in age from 12 to 75 years, and in each case there was hypertrophy of the pylorus.

Maylard [12] described seven cases in which he operated because of symptoms that suggested peptic ulcer, but instead of ulcer he found stenosis of the pylorus. Gastro-enterostomy relieved the symptoms in each case.

Mayo-Robson and Moynihan [13] quoted Maier [11] and referred to a case of Hussey's [14] in which gastro-enterostomy relieved the patient. They described a case of their own in a man, aged 24, in whom symptoms of gastric retention had progressed insidiously for five years. Exploration revealed a tightly contracted pylorus. It was dilated manually, and the patient had no further trouble for three months. At the end of that time, the symptoms recurred. Another operation was advised, and at that time a gastro-enterostomy was made, which gave permanent relief.

Bastianelli [15] described four cases in which there was pylorospasm but no retention of gastric chyme. Exploration showed thickening of the pylorus with slight evidence of a low grade inflammation but no ulceration. The Rammstedt operation was employed successfully.

Bianchetti [16] recorded a case in which he resected a thick pylorus which seemed to be malignant. Microscopic examination of the specimen, however, revealed only marked hypertrophy of the circular muscle

10. Freeman, Leonard: Discussion, Ann. Surg. **90**:540, 1929.

11. Maier, R.: Beitrage sur angebornen pylorus stenosis, Virchows Arch. f. path. Anat. **102**:413, 1885; quoted by Maylard (footnote 12).

12. Maylard, A. E.: Congenital Narrowness of the Pyloric Orifice a Cause of Chronic Gastric Disease in the Adult, Brit. M. J. **1**:416, 1904; **1**:626, 1920.

13. Mayo-Robson, A. W., and Moynihan, B. G. A.: Diseases of the Stomach and Their Surgical Treatment, New York, William Wood & Company, 1904, p. 522.

14. Hussey, quoted by Mayo-Robson and Moynihan (footnote 13).

15. Bastianelli, R.: Pylorus Spasm and Its Surgical Treatment, Ann. Surg. **81**:45, 1925.

16. Bianchetti, C. F.: Contributo allo studio della stenosi pilorica ipertrofica idiopatica dell' adulto, Arch. ital. di chir. **15**:585, 1926.

fibers, which he called "circular myoma." Crohn [17] reported one case in which a Rammstedt operation was used successfully, and Chaney [18] described another in which a Horsley pyloroplasty gave satisfactory results. Martin and Burden,[4] in reporting cases of pyloric achalasia, called attention to the frequency with which the symptoms of achalasia simulated those of peptic ulcer, particularly the early stage of ulcer.

COMMENT

The pathogenesis of hypertrophic pyloric stenosis in adults is an interesting subject for conjecture. There are two possible origins; namely, it may arise de novo in entirely normal persons, or it may represent activation of a previously quiescent but already hypertrophied or spastic pylorus. Clinically there are varying degrees of congenital hypertrophic pyloric stenosis, and it does not seem unreasonable to suppose that there may be so little stenosis in some infants at birth that they may pass through infancy, childhood and a part of adult life without trouble. Something in the intrinsic or nervous mechanism of the pylorus goes wrong, and symptoms appear.

Stenosis of the pylorus arising de novo in a previously normal person with a properly functioning pylorus seems improbable and difficult to explain on any basis other than that of imbalance of the autonomic nervous system. It is possible, however, that abnormal nervous stimuli or an abnormal response to stimuli may cause pylorospasm, and that a long continued spasm may cause hypertrophy. Because of the incompleteness of the data on the subject, however, it is difficult to discover the etiology in each case.

The diagnosis of the condition should not present great difficulties. Were it borne in mind and considered more frequently when patients are examined who complain of vague or atypical symptoms in the upper part of the abdomen, fewer cases would go unrecognized. The frequency with which the symptoms resemble those of peptic ulcer, particularly the early stage of ulcer, has already been mentioned. One of my cases falls in this category, the other two patients complained of relatively constant discomfort and soreness rather than of actual pain in the epigastrium. There was an accompanying sensation of fulness. Two of the patients complained of nausea and vomiting periodically, and two had lost from 25 to 30 pounds (from 11.3 to 13.6 Kg.). Physical examination did not reveal any typical changes.

The final diagnosis must be made roentgenologically. Constant spasm of the pylorus with more or less lengthening and narrowing of

17. Crohn, B. B.: Congenital Pyloric Stenosis in Adult Life, J. A. M. A. **90**:197 (Jan. 21) 1928.

18. Chaney, R. H.: Congenital Pyloric Stenosis in Adult Life, J. M. A. Georgia **17**:57, 1928.

the lumen of the pylorus is presumptive evidence, and when accompanied by signs of gastric stasis or retention is conclusive evidence of the presence of pyloric stenosis. That gastric stasis is not a constant feature of such cases, however, was stressed by Bastianelli. The degree of hypertrophy may be difficult to determine but is not in itself of major importance. It seems probable that in the past many of these cases have been diagnosed "pylorospasm," and dismissed as neurasthenic cases.

The treatment prescribed must depend on the severity of the syndrome and the degree to which the patient suffers discomfort and incapacity. In all except the mildest cases, in which antispasmodics and small, frequent meals might be given a trial, surgical treatment seems to be indicated. In my cases, one patient was treated by manual dilation of the pyloric sphincter. As in the case cited by Mayo-Robson and Moynihan, temporary relief from symptoms ensued, but the original discomfort recurred after a few months. In the other two cases, plastic operations on the pylorus were performed, and were followed by complete and permanent relief. The importance of prompt surgical treatment in such cases is suggested by the evidence of inflammation which is present in the tissues about the pylorus under these circumstances. That spasm of the pylorus may be of etiologic significance in the formation of peptic ulcer has been suggested already by others and myself.

The type of operative procedure to be employed is probably more a matter of personal choice than anything else. The Rammstedt, Heineke-Mikulicz, Judd, Horsley or Martin-Burden type of plastic reconstruction of the pylorus may be used to advantage. There is much to be said, however, in favor of the operation by which the major portion of the pyloric ring is actually excised, and parts of the adjacent stomach and duodenum are interposed between the severed ends of the sphincter. This type of operation leaves a funnel-shaped communication between the stomach and the duodenum with the minimum possibility of subsequent cicatricial constriction.

SUMMARY

I have called attention to a syndrome that seems to constitute a rather definite clinical entity. It is characterized by hypertonicity and hypertrophy of the pylorus with narrowing of its lumen, as was illustrated by the histories of the three cases reported. After a brief survey of the rather small amount of literature on the subject, these cases were discussed from the standpoint of the pathogenesis, diagnosis and treatment. A plea is made for the recognition of this condition and its consideration in the diagnosis of all vague or atypical symptoms referable to the upper part of the abdomen. The final diagnosis must be made roentgenologically, and the importance of surgical treatment and the types of operations to be used are referred to briefly.

CHRONIC CYSTIC MASTITIS

PRELIMINARY REPORT ON THE NATURE OF THE PROCESS *

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Ten years ago in a paper [1] read before the surgical section of the Southern Medical Association, I made certain dogmatic statements concerning chronic cystic mastitis and other, as I then believed, definitely precancerous lesions of the breast. One of the penalties of increased experience is often that one can no longer be quite so sure, and so it is with our present-day belief concerning the nature of this process called by many names but perhaps most often, chronic cystic mastitis. The main issue is now what it was then, an appreciation of the importance of this condition with relation to its malignant tendencies.

I do not believe that my own experience, with due regard for that of others, entitles me any longer to look on this process as definitely precancerous, as I thought it was ten years ago, and in fact until recently. That it does at times lead to carcinoma there can be no question, but, it does not do so nearly as often as was formerly thought. I cannot feel, therefore, that the surgeon is justified in doing the radical operation for this condition with the same security of belief that in so doing he is forestalling the development of cancer. There can be no doubt that many breasts have been needlessly excised because of this belief. The difficulty, however, lies in the fact that some of the cases become malignant, and it is impossible to say with any certainty which ones will do so. One must therefore be guided entirely by the case at hand and not by a set of rules. One must not be too much influenced by the specter of cancer in the offing. If each case of breast irregularity with respect to age, menstrual and sexual history, together with what is now known of the physiologic cycle of breast tissue behavior, is carefully considered, one can usually decide on the best procedure for that given case. The most important of these factors in women of child-bearing age is the menstrual function. The amount of involution and evolution which the breast undergoes during its active life is great, no other organ being given to more epithelial unrest.

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* Read before the Section on Surgery at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 10, 1929.

1. Rodman, J. Stewart: Pre-Cancerous Lesions of the Breast with Special Reference to Chronic Cystic Mastitis, South. M. J. **13**:348 (May) 1920.

It is, of course, impossible to understand the pathologic changes in an organ if one fails fully to appreciate its physiology. The mammary gland, as is now known, is similar in the two sexes up to the age of puberty, but from then on fulfils its real function only in the female. These astonishing epithelial and fibrous tissue aggressions and regressions occur only in women and at times give rise to great difficulty in deciding between the normal and the abnormal.

We now believe that when this normal involuntary cycle in the breast is interfered with, disease begins, and that adenoma, fibroadenoma, papillary cyst adenoma, chronic cystic mastitis and even carcinoma may develop. It is, in reality then, one process with variations of the theme.

My continued interest in this subject clinically has given me the opportunity of seeing tumors of the breasts entirely disappear, which were not operated on because of a growing conservatism. This is a dangerous doctrine unless one has had a reasonably large experience in the matter, because valuable time might be lost in doing the radical operation to forestall the development of, or to attempt to cure a case of, early cancer. The surgeon must work hand in glove with a competent pathologist who has a special interest in the subject.

Recent literature justifies one in more conservative practice than that to which surgeons have been accustomed in the past. As long ago as 1907, Hitschmann and Adler [2] described the endometrium in the different stages of the menstrual cycle and thus threw new light on lesions of the uterus. It is known that these changes are correlated with the development and the regression of the corpus luteum. This work has a definite analogy to physiologic changes in the breast tissue as was shown in 1922, by Rosenburg,[3] who found in cut sections of the breast and the uterus, in cases coming to autopsy, a similar sexual cycle in the mammary gland. Polano and Sedening confirmed these observations in cases from the surgical clinic, but they denied that postmenstrual regression is always complete. Cheatle,[4] McFarland [5] and others have shown that what has

2. Hitschmann and Adler: Wien. med. Wchnschr. **57**:1297, 1907; Monatschr. f. Geburtsh. u. Gynäk. **27**:1, 1908; Arch. f. Gynäk. **2**:233, 1913.

3. Rosenburg, A.: History of Breast During Normal or Disordered Menstruation, Virchows Arch. f. path. Anat. **262**:298, 1926.

4. Cheattle, G. Lenthal: Cysts and Primary Cancer in Cysts of the Breast, Brit. J. Surg. **8**:149, 1920; Benign and Malignant Changes in Duct Epithelium of the Breast, ibid. **8**:285, 1921; Cancer of the Breast, Brit. M. J. **1**:869 (June) 1922; Hyperplasia of Epithelial and Connective Tissue in the Breast: Its Relation to Fibroadenoma and Other Pathological Conditions, Brit. J. Surg. **10**: 436, 1923; Desquamative and Dysgenetic and Epithelial Hyperplasias in the Breast, ibid. **13**:509, 1926; Early and Late Carcinoma of the Breast, Practitioner **116**:281 (April) 1926; 337 (May) 1926; Chronic Mastitis, Cysto-Adenoma and Adenoma of the Breast, Arch. Surg. **17**:535 (Oct.) 1928.

5. McFarland, Joseph: Adenofibroma and Fibro-Adenoma of Female Breast, Surg. Gynec. Obst. **45**:729 (Dec.) 1927.

been considered a pathologic process is in reality probably nothing more than aberrant physiology.

I have succeeded in enlisting the interest of my colleague, Dr. Helen Ingleby, Professor of Pathology at the Woman's Medical College, in this subject and the pathologic data in some of my recent cases are hers. I have labeled this a preliminary report, because time has not permitted a careful search of all of my past cases from this point of view. I feel justified, however, in the light of what has been written and of what a review of some recent cases has shown in making these statements at this time, realizing that in so doing I am going back on my printed words of the past, but one is justified at times in changing one's mind, even in scientific matters.

Although the subject is chronic cystic mastitis, I believe that no adequate discussion of the subject can be entered into without first briefly considering some of the more recent additions to physiologic knowledge of the cycle of the mammary gland, as well as other variations from the normal, such as adenoma, adenofibroma, fibro-adenoma and papillary cyst adenoma.

Somewhere between the menstrual cycles the breast is in its resting stage, probably from the fifth to the fifteenth day after the last menses. At this time the fibrous stroma predominates, the epithelial elements are only ducts and occasional acini. In old women and obese young women fat is also present. The ducts are lined by two layers of cells; an inner layer of cuboidal or columnar with nuclei that are small and stain deeply; and the basal cells that are smaller, and tend to be flattened. As the next menstrual period approaches, the cells become larger until they divide and new ductules are formed branching out from the old ducts like twigs on a tree. The epithelial border around the lumen becomes somewhat jagged and irregular, a change similar to that seen in the glands of the premenstrual endometrium. Meanwhile the surrounding fibrous tissue also softens, undergoing myxomatous and hyaline degeneration so as to allow for the expansion of the ducts. Lobules are thus formed which do not appear in the resting breast. The lining epithelial cells swell, the protoplasm becomes vacuolated and the nucleus is rounder and paler. Similar changes take place in the cells of the basal layer. Secretion takes place into the ducts and, clinically, in many women the breasts become swollen and tender at this stage. This then, is the premenstrual phase, and about a day or two before the onset of the menstrual flow, involution begins. At this time the epithelium degenerates and is shed into the lumen of the ducts much the same as the superficial layers of the endometrium are cast off during menstruation. Under the microscope, it is seen that the architecture of the lobules has been lost, and they have a curiously jumbled appearance.

One now sees degenerate epithelial cells, often varying in size and shape, intermingled with round cells and proliferating fibrous tissue. After the menses are over these degenerated epithelial cells are absorbed. The breast is now in the postmenstrual phase which is short, as in about five days after the menses the breast again enters the resting stage.

If pregnancy intervenes, lactation changes begin. The breast hypertrophies in the same way as it does in the menses, but to a much greater extent. Numerous new acini are now formed and the periductal fibrous tissue is pushed aside, and is no longer distinguishable from the perilobular connective tissue. It is here that the epithelial activity, of course, is at its height. After lactation is over involution occurs, hyperplasia ceases, secretion is absorbed and the empty acini collapse because of the pressure of the elastic tissue on their walls. Most of the acini disappear at this time but the gland never returns quite to the normal virgin state. Lactation hypertrophy, both of the fibrous and the epithelial elements, remains to some extent. After the menopause further involution occurs.

It is of prime importance that a surgeon have complete data of the menses and sexual life of the patient under treatment, as I have seen what enormous differences can be expected in the premenstrual, postmenstrual, resting, lactating, postlactating and senile breasts. The amount of new growth taking place in the mammary gland at each sexual cycle is astonishing. Premenstrual proliferation is much more rapid than carcinomatous growth. In all probability, a hormone from the anterior pituitary body controls the secretion from the graafian follicle and the corpus luteum of the ovary, which in turn controls the growth of breast tissue. Moszkowicz [6] believes that growth and regression during the sexual cycle in the breast can sometimes be traced to ovarian dysfunction, and that the ovaries exert a controlling influence over evolution and involution of the gland.

What aberrations might be expected if proper growth and involution were interfered with? Such interference might be local or generalized in the breast tissue. Either epithelium or fibrous tissues, or both, might take part in the aberrant process. It has been shown that local changes occur in the uterine mucosa when inadequate development of the graafian follicle causes a chronic but localized hyperplasia of the endometrium. Such a localized process in the uterus becomes a uterine polyp. I believe that chronic local hyperplasia in the breast results in an adenoma—adenofibroma if the epithelial elements are affected as well as the fibrous tissue, fibro-adenoma if the fibrous tissue predominates. If the epithelial cells come to a stage of secretion, and the normal absorption is for some

6. Moszkowicz, L.: Sexual Cycle, Mastopathy and Tumor Growths of Female Breast, Arch. f. klin. Chir. **144**:138, 1927; Cystic Disease of Breast as Precancerous Epithelial Proliferation, Virchows Arch. f. path. Anat. **262**:531, 1926.

reason interfered with, cysts of the acinar type will occur. It appears that cells shed normally into the lumen of the ducts in the postmenstrual phase, do not pass in large quantities from the nipple, as it is known that such a discharge during menstruation is rare. If the fibrous tissue was chiefly affected, the ducts would try to proliferate as they do normally in the premenstrual phase, but they would be pressed on and pulled out by the fibrous tissue, and result in the ordinary intracanalicular type of fibro-adenoma. If this process is carried further, the ducts become invaginated and there results a series of projections within the lumen of the cavity covered by epithelium. If the ducts are distended by unabsorbed secretion, the result is a papilloma.

One of the essentials of a benign tumor is that it must have a capsule. In many of McFarland's cases and in some of mine, careful pathologic examination did not reveal a true capsule, even though the surgeon felt that there was one at the time of its excision from the surrounding breast tissue. Many of the tumors are semi-encapsulated, showing complete continuity with a normal breast on one side and sharp demarcation from breast tissue on the other. In some of the cases of localized aberrant physiology, the proliferation of the fibrous and epithelial elements has been sufficiently great to push the surrounding fibrous tissue aside to form a capsule. If there is no attempt at localization, and the same changes are widespread, one finds chronic cystic mastitis or the abnormal involution of Warren, which I now believe to be the best of the many names suggested. Moszkowicz has grouped the aberrant physiologic changes under the term "mastopathy," but I cannot believe that for clinical usage this term will find as much favor as that of Warren. It is true that some of these changes have to do with abnormal evolution rather than involution, but in the majority, involution is at fault. It is certainly a tribute to Warren's original observations on this disease made many years ago that, in my opinion at least, the name that he gave it is still the best.

There can be no doubt that carcinoma may develop in a breast showing abnormal involution. We do not believe now, however, that it happens nearly so frequently as we formerly thought, or that cause and effect have the same direct bearing. Carcinoma, however, when its origin can be traced, seems to arise in larger ducts, not in lobules, and we now believe that while this condition of abnormal involution may prepare the ground, so to speak, that in the vast majority of cases nothing further than the aberrant physiologic changes occur. Unfortunately, microscopic examination does not disclose whether a given lesion of the breast is carcinomatous or not, until it is advanced. Pathologists, I believe, agree that there is absolutely no way of recognizing a carcinoma cell other than by its behavior.

CONCLUSIONS

1. The first essential in dealing with breast irregularities is a real appreciation of the astonishing amount of epithelial and fibrous changes that normally occur during the premenstrual, postmenstrual, lactation, postlactation, menopause and senile phases.

2. During the active phases of the life cycle of the gland, it is necessary that one has accurate data concerning the time of the menstrual period, in its relation with the appearance and development of the tumor in question, as well as all other data which will put the case in point into one of the phases given.

3. Conservatism is justifiable in dealing with abnormal involution, provided one fully appreciates the somewhat rare development of carcinoma in such cases. Any tumor that does not change with local treatment (support and mild counterirritation) after one menstrual period has been passed should be removed by local excision and submitted to a frozen section, the pathologist choosing the part to examine microscopically.

5. If there is reasonable doubt in the mind of the pathologist who has made this subject one of special interest, after microscopic examination of the frozen section, the surgeon should proceed with the radical operation as for carcinoma.

6. Regardless of the vast amount of interest which this subject has aroused in the past, considerably more evidence from experimental, detailed physiologic and pathologic sources is necessary before some of the statements made in this paper can be confirmed.

ABSTRACT OF DISCUSSION

Dr. A. R. Kilgore, San Francisco: I have long felt that the cause of chronic cystic mastitis would be found bound up with internal gland hormone dysfunction. Chronic cystic mastitis (abnormal involution) can be divided into two quite distinct types in such a manner as to simplify the problem of its relation to cancer. The one universal characteristic of all stages and types of abnormal involution is an increase in the number of individual gland units. The first stage in the involution may be shown as a simple increase in number of acini, the lobules being larger than normal and closely packed. With dilatation to form cysts, the epithelial lining may react in two ways. It may either remain smooth and eventually become atrophied or entirely disappear, or the epithelium may be thrown into hyperplastic folds and eventually into a papilloma, composed of almost solid, atypical epithelium. Cancer would not be expected from atrophied or absent epithelium, and I believe it is now generally accepted that cancer occurs in connection with the smooth-walled cyst of the first type only as a rare incident. Cancer would not be unexpected, and, I believe, does arise from hyperplastic epithelium. In the laboratory at the San Francisco Hospital, there is a small group of thirty-five specimens of the nonhyperplastic type, none of which presented cancer at operation. There are nine more or less extensive tumors of the hyperplastic type (nonencapsulated cystadenoma) in four of which cancer had already developed at the time of opera-

tion. In three of these four cases the presence of cancer was proved by metastasis or by later known death caused by cancer. Cancer not being found at operation in one type and such a high proportion presenting cancer already developed in the second type strongly suggest that the hyperplastic type of abnormal involution is a definite precancerous condition.

DR. J. S. HORSLEY, Richmond, Va.: Dr. Rodman's paper and Dr. Kilgore's discussion have been illuminating, and have helped to clarify the subject of chronic cystic mastitis, which has been much confused and misinterpreted. To say, on the one hand, that there is no connection between chronic conditions such as this abnormal involution in which there is sometimes a distinct tendency toward hyperplasia of the epithelium and toward cancer, and, on the other hand, to say that certain types of abnormal involution, in which there is no hyperplasia of the epithelium, have a tendency to cancer, is illogical. One extreme is as bad as the other. One knows that in other regions of the body chronic processes, whether one calls them inflammatory or not, that are accompanied by a hyperplasia of the epithelium, tend toward malignant conditions in some instances. There are, of course, exceptions. For instance, primary cancer practically never develops on the soles or on the palms, even though the palms are subject to frequent trauma, probably more than any other region of the body. It seems that this exception may be due to biologic reasons or to the fact that the two tissues have been subject to trauma in evolutionary times and have acquired a marked stability. After all, the cancer cell is the result of instability of the tissue, and of the inability of the tissue to control its constituent cells. When the stability is marked as in the palms and soles, no amount of trauma seems able to cause that chaotic condition which is cancer. In comparatively modern conditions, modern from a biologic standpoint, trauma, or chronic processes that appear to accompany civilization or result from it, frequently do not have the proper biologic corrective influence that is necessary to keep the cells within bound. I think it is undoubtedly true that, occasionally there is cancer in connection with chronic cystic mastitis or abnormal involution. I have had one or two cases of my own which I think are quite definitely pathologically proved, but to do a radical operation in practically all of the cases is unnecessarily mutilating surgery. It seems to me that the grounds that have been recommended by Dr. Rodman and suggested by Dr. Kilgore are admirable.

DR. J. S. RODMAN, Philadelphia: I am in entire agreement with Dr. Kilgore and Dr. Horsley, and wish to thank them for their discussion.

A REVIEW OF UROLOGIC SURGERY

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LOS ANGELES

KIDNEY

Anomalies.—Bagg [1] reported the results of experimental studies dealing with the effect of roentgen and radium treatment for certain congenital hereditary abnormalities of the genito-urinary organs that were found in laboratory animals. His data have been collected during the last six years and are based on records of 5,600 necropsies, especial attention having been given to selective breeding for renal defects. One thousand and fifty-seven animals had defects of the kidney. There were 1,000 animals, 519 males and 481 females, with one or both kidneys missing. One kidney was absent in 630 animals, and both kidneys were absent in 334 animals. Twenty-five animals had a solitary kidney which was reduced in size. Thirty-five animals had one hydronephrotic and one normal kidney. There were 11 animals with one hydronephrotic kidney; the other was not present. This summary also considered 17 animals in which one or both testes were abnormal. The elimination of a testis after birth has been traced to diffuse hemorrhagic extravasation within that organ, a condition which was noted a few hours after birth, and the same testis was missing at necropsy several months later.

Well marked anatomic abnormalities have appeared in the descendants of male and female mice that have been submitted to treatment with roentgen rays; the defects breed true, are recessive in character and behave mainly as mendelian in inheritance. These studies are of clinical significance in indicating that caution should be used in irradiation over the region of the ovaries when the patient is pregnant.

1. Bagg, H. J.: Hereditary Congenital Anomalies of the Genito-Urinary Organs, Am. J. Surg. **7**:211, 1929.

This caution also applies to irradiation of the gonads in men when the product of these organs may enter into a pregnancy at some later date.

Only the parent generation animals, both males and females, were irradiated. The first type of abnormality to be found was the presence of congenital defects of the eye in certain of the unirradiated descendants in the third and subsequent generations. It has bred true for nineteen generations over a period of six years. In still later generations peculiar forms of defects of limbs made their appearance, clubbing, syndactylism, hypodactylism and polydactylism being the most prominent types. By selective breeding these abnormalities have also been intensified so that in certain litters as many as seven of eight young have shown one or more defective limbs.

The first type of defect of the kidney was noted when necropsy was performed on animals of the fifth generation that were descendants of the group that had been irradiated. Some of these animals had a so-called solitary kidney defect. By breeding males and females of this group, the relative frequency of incidence of this abnormality was raised from 16.75 per cent in unselected animals to 57 per cent in litters in which both parents had the solitary kidney defect.

Stones.—Chwalla [2] reviewed 143 cases of renal stone and 91 of ureteral stone from the city hospital of Vienna. Sixty per cent occurred in men and 40 per cent in women. Substantiating Israel's observation, there were twice as many ureteral stones in men, and only 20 per cent more renal stones. Forty-one per cent were on the right side, 46 per cent on the left and 13.6 per cent were bilateral. Among the 55 cases of ureteral calculi in men, 65 per cent were in the pelvic portion of the ureter, 12.7 per cent in the iliac and lumbar portions and 9 per cent just below the renal pelvis. Among the stones in the lower part of the ureter, 19 were intramural and 15 were in juxtaposition to the bladder. Of the 26 cases of ureteral stone in women, 19 (73 per cent) were in the pelvic region, 2 (7.7 per cent) were in the iliac region and 5 (19 per cent) were in the upper part of the ureter. Stones were not observed in the lumbar region of the ureter. In 13.5 per cent of the cases the stones were multiple. Lithiasis is chiefly a disease of the third and fourth decades, and is sometimes observed in the first and seventh decades.

Chwalla concluded that the output of indigo carmine (sodium indigolindisulphose) does not give an accurate indication of the degree or extent of the pathologic process present. Even in markedly changed kidneys function may recover after removal of the stones. Large hydronephrotic kidneys (associated with stones) were noted to return

2. Chwalla, Rudolf: Das Spätschicksal unserer Nieren- und Ureterstein-fälle, Ztschr. f. urol. Chir. **26**:157, 1929.

to normal capacity after a period of years. Observations did not show that a kidney in this condition had any reflex or toxic influence on a normal kidney. In most cases, following pyelolithotomy, nephrolithotomy, pyelonephrolithotomy or ureterolithotomy, the indigo carmine output of the affected kidney is likely to become almost normal soon after operation. In cases in which this does not occur there is usually a recurrent stone or a remaining stone, but seldom a badly injured kidney.

Recurrent or overlooked stones are the most common cause of the continuation of an infection following operation. Seventy-two and two-tenths per cent of the cases of renal stone and 70.2 per cent of the cases of ureteral stone were traced. In 31.75 per cent of the cases of ureteral stone there were definite signs of recurrent calculus on one side or the other. There was an incidence of recurrence in cases in which operation was performed of at least 8 per cent following pyelolithotomy, 36.3 per cent after nephrolithotomy and 7.4 per cent following ureterolithotomy. Following nephrectomy there was an incidence of 16.2 per cent of stones in the remaining kidney. These data show that there is an average of at least 18.5 per cent recurrence of stones.

[Compilers' Note.—Much has been written recently on recurrence of renal stones. Cifuentes [3] found recurrence of stones in only 2 per cent of aseptic cases. Rovsing [4] reported statistics relative to infection and recurrence. In 44 (40.3 per cent) of 109 cases of nephrolithotomy, there was a recurrence; 58 were aseptic cases, of which only 15 (25.8 per cent) recurred. Nephrolithotomy was performed in 27 cases of infected urine; there was recurrence in 10 (37 per cent). In 19 (79 per cent) of 24 cases in which there were micro-organisms of decomposing urea there was recurrence. There were only 7 cases of pelviolithotomy, and in 2 of these the disease recurred. Sixty-eight per cent of all recurrences occur in infected kidneys. It is interesting to compare Rovsing's figures with those in a series of cases reported by Braasch and Foulds.[5] Recurrence followed in 44 (11.8 per cent) of 375 cases after pelviolithotomy, 25 (24 per cent) of 104 cases after nephrolithotomy and 2 (4.1 per cent) of 48 cases after combined nephropelviolithotomy.

Rafin [6] reported a series of cases in which lithiasis recurred after pyelotomy in 23 per cent of the cases, after nephrotomy in 15 per cent and after primary nephrectomy in 3.3 per cent. In the combined series

3. Cifuentes: III. Sitzung: Fernresultate der Operationen wegen Nephrolithiasis, Ztschr. f. urol. Chir. **16**:169, 1924.

4. Rovsing, C. M.: Infection as Cause of Recurrence Following Operations for Kidney Stone, Acta chir. Scandinav. **57**:387, 1924.

5. Braasch, W. F., and Foulds, G. S.: Postoperative Results of Nephrolithiasis, Tr. Am. A. Gen.-Urin. Surg. **16**:155, 1923.

6. Rafin: Valeur comparée des diverses interventions pour lithiase rénale, J. d'urol. **18**:523, 1924.

lithiasis recurred after pyelotomy in from 0 to 25 per cent of the cases (aseptic) and in from 7 to 50 per cent of the cases (septic); after nephrotomy in from 3.2 to 17 per cent of the cases (aseptic), and in from 7 to 54 per cent of the cases (septic), and after nephrectomy in from 1 to 4 per cent of the cases.]

Thompson [7] studied necropsy records of 12,888 cases in order to review the question of the formation of stones in the kidney and ureter. In this series some lesion occurred in the urinary tract in 2,200. Calculus formed in 162 cases. The incidence of the formation of stone was approximately equal in the two sexes, especially during the first decade of life. From the ages of 11 to 40, lithiasis was more common among women than men, but from the age of 41 its occurrence was greater in men. Stone is more commonly found on the right side than on the left in both sexes, and is more commonly located in the pelvis or calices of the kidney than elsewhere in the urinary tract.

Thompson commented on what he termed "travelling stone;" that is, a stone in the kidney which passes along the ureter and into the bladder, then through the urethra. Bearing in mind the data noted at necropsy, he concluded that stones travel more frequently in women than in men, and he noted in his clinical experience that a stone is impacted in the right ureter more commonly than in the left in men.

In a third of the cases the stones formed on both sides. Thompson did not give much credence to the idea that hypertrophy of the kidney on one side results in response to disease of the opposite side, and considered that this is less common than is generally thought. Stones may recur after operation for their removal, a condition usually due to careless or incomplete removal of the calcareous materials. In three cases the stone was associated with new growth and apparently was the causative factor in its formation.

Quinby [8] stated that unless there are external contraindications, all renal calculi which are too large to pass through the normal channels should be removed surgically. The aim of such operation should be to remove the stone with as little destruction of renal tissue as possible, with free drainage of the kidney assured. Free mobilization of the kidney, together with the use of roentgenograms made at the operating table, makes it possible to cope with the problem presented in whatever way seems best. The simplest attack on the kidney is that of pyelotomy; the next in severity is pyelonephrotomy and the most severe is extensive nephrotomy. Nephrectomy should be performed only in cases

7. Thompson, A. R.: Renal and Ureteric Stone Formation, Guy's Hosp. Rep. **79**:173, 1929.

8. Quinby, W. C.: The Operative Treatment of Renal Lithiasis, Am. J. Surg. **7**:234, 1929.

in which the kidney has been rendered valueless by the disease. After all obvious concretions have been removed, further search by roentgen examination should be made in order to be sure that no particles remain to serve as the nucleus for subsequent formation of stone. Particles are best removed by washing and by the use of the negative pressure tube. A final roentgenogram should show the kidney entirely free from shadow-casting material. Patients should be closely observed after operation, and every effort should be made to restore the urinary passage to a sterile condition.

Graves [9] reported a case to illustrate the rapidity with which renal stones may develop in some cases. The patient, a man aged 29, complained of recent acute pain. Examination revealed a stone 1 by 0.5 cm. in the middle of the left ureter, with incipient hydronephrosis above it. A roentgenogram also showed the shadow of a minute concretion apparently in the cortex of the kidney on the right side. Infection or other demonstrable abnormality of the urinary system was not present. The ureteral stone was removed. Eighteen months later, the patient returned with recurrent pain. Roentgenograms showed a large renal calculus on the left side, associated with several smaller stones. The urine from the left kidney was infected with *Staphylococcus aureus*. The small fragment of stone in the cortex of the right kidney had not changed in size and position as compared with the previous examination. Left nephrectomy was necessary because of the stones and the extensive infection throughout the organ. Convalescence was satisfactory.

[Compilers' Note.—The question of the time necessary for the formation of urinary calculus has been debated by many urologists. Stones in the bladder occasionally arise rapidly, particularly when a foreign body such as a catheter or a suprapubic tube is present. Instances of formation of stone 4 or 5 cm. in diameter have occurred over a period of from six to seven weeks, between the stages of prostatectomy. Cases have been reported of stones in the kidney growing to 1 cm. in diameter in two months. In one case a stone was observed over a period of five years. At the onset it was 6 mm. in diameter; five years later it completely filled the pelvis, with destruction of the kidney and marked reduction of function, necessitating nephrectomy.]

Eisendrath and Arens [10] considered the difficulty in distinguishing between shadows of biliary and renal calculi on account of the anatomic

9. Graves, R. C.: Rapid Formation of Renal Calculus, New England J. Med. **200**:421, 1929.

10. Eisendrath, D. N., and Arens, R. A.: Pyelography and Cholecystography as Aids in the Differentiation of Shadows Due to Renal or Biliary Calculi, Surg. Gynec. Obst. **49**:1, 1929.

proximity of the gallbladder and kidney in normal persons. The radiographic opacity of any calculus depends on the atomic weight of the constituents and the structure and thickness of the calculus. Soft calculi are much less opaque than hard calculi. The range of migration of biliary stones is usually greater than renal or ureteral calculi, except in cases in which the latter have formed in a dilated renal pelvis or ureter or both. Cholecystography or pyelography or the combination of these two methods is a valuable diagnostic aid in distinguishing between biliary and renal stones. Eisendrath and Arens make multiple exposures by rotating the patient, because in some instances the suspected calculus may appear to lie in the gallbladder or kidney, while in others its true position is at once evident.

The opacity of urinary calculi decreases according to the following: calcium carbonate, calcium oxalate, calcium phosphate, magnesium phosphate, uric acid and urate, cystine and xanthine and fibrin.

[Compilers' Note.—With the advent of cholecystography came another method of differentiating shadows of renal and biliary origin. Eisendrath previously reported cases illustrative of the value of the combined use of the pyelogram and cholecystogram. As the shadow of the gallbladder and the pyelogram are found at times to overlap and to include the shadow of stone, the situation may still be confusing; thus the use of multiple exposures at different angles, with rotation of the patient. Pyeloscopy of manipulation of the iodide-filled renal pelvis under the fluoroscope, as is being developed by Braasch, could probably be applied with value in some of these cases. One can at once see the importance of using both pyelography and cholecystography in conjunction when shadows in the upper right quadrant of the abdomen lead to confusion.]

Tumor.—Plaut [11] reported the case of a woman who had had calculi in the renal pelvis, and in whom the epithelium of the pelvis and part of the ureter were cylindric. The epithelium of the mucous membrane formed glands which connected with an underlying stroma imitating the structure of the intestinal wall. At the same time the muscle tissue became hyperplastic. A portion of this probably originated from destroyed blood vessels and part from the wall of the renal pelvis or from the renal papillae. The influence of infection in this process cannot be determined. Renal atrophy resulted from the concerted pressure of the pus, mucus and tumor. Some of the tubules appeared to have regenerated, and there were areas similar to the renal blastoma.

11. Plaut, Alfred: Diffuses dickdarmähnliches Adenom des Nierenbeckens mit geschwulstartiger Wucherung von Gefässmuskulatur, Ztschr. f. urol. Chir. **26**: 562, 1929.

The tumor described cannot be identified by the literature. It has some characteristics similar to exstrophy of the bladder. The similarity to intestinal structure must designate it as blastoma. Terms such as heteroplasia, protoplasia and metaplasia do not seem to explain the pathogenesis. The presence of the renal stone and the severe infection can scarcely be etiologic factors. To explain the diffuse extension through the ureter, pelvis and calices, multiple points of origin must be considered.

Hunt and Hager [12] reported that of 271 cases of malignant renal tumors in which the patients were operated on in the Mayo Clinic over a period of ten years, 241 were traced. In a group of 225 cases of adenocarcinoma, 199 were traced. In 177 nephrectomy had been performed and in 22, exploration. Of the 199 patients traced, only 73 are living; 62 were alive after three years; 37 after five years, and only 3 after ten years. There were 21 operative deaths. The presence of a palpable tumor was not found to influence the final result, unless the size produced difficulty in operations. Radiotherapy was given in many cases, but it was difficult to estimate whether benefit was derived from it.

There were 10 patients with sarcoma, 8 of whom were traced. The average age of the patients was 47 years. The tumors were large, and in the pyelograms it was difficult to distinguish between renal and extrarenal tumors. Nephrectomy was performed on 7 patients, only 2 of whom are alive. One was operated on two and a half years later for secondary growth; the other was healthy at the end of three years. Radiotherapy was given with no proved beneficial result.

Malignant tumors occurred in 13 children, 11 of whom were traced. The ages ranged from 20 months to 7 years. All had palpable tumors, 8 on the right side and 3 on the left. One patient is alive and healthy seven years later, and another two years later, with signs of recurrence. It was doubtful if radiotherapy affected the results.

Twenty-three patients had epithelioma of the pelvis. Of 12 patients traced, 8 had died. One lived as long as nine years.

[Compilers' Note.—The poor results of radiotherapy in dealing with any type of renal neoplasm, the ominous outlook for sarcomatous patients with any form of therapeutic attack, and the relatively bad prognosis for malignant renal tumors in children summarize the conclusions of these authors, which are in accord with the opinions of most investigators.

The earlier the treatment is instituted, the more extensive the operation, and the more the tumor corresponds to the type of adenocarcinoma

12. Hunt, V. C., and Hager, B. H.: A Review of 271 Cases of Malignant Renal Neoplasms, S. Clin. N. Amer. 9:149 (Feb.) 1929.

or hypernephroma, the more the chance of cure by radical surgical procedures. As for degrees of malignancy, the pure sarcoma and carcinoma usually rank first, the mixed cells of Wilms' tumors seen in children, next, and last, the hypernephroid types. The relatively better outlook in dealing with early epithelioma of the renal pelvis is shown by Hunt and Hager's cases.]

Hydronephrosis.—Mezö [13] considered various methods of reconstructing hydronephrotic renal pelves, among which he mentioned plication, ureteropelvic anastomosis and reimplantation. In a normal physiologic condition the ureter is inserted into the deepest portion of the pelvis, while in hydronephrosis it is often inserted at a higher point. The object of the different operative measures is to repair so as to eliminate any residual urine in the renal pelvis. These operations rarely are successful, even in uninfected cases. The formation of fistula or of perinephric abscess usually results, and in many cases secondary nephrectomy becomes necessary.

In some cases "transversopexia" had aided in the treatment for the hydronephrosis. In this procedure the urinary tract is not disturbed; the kidney is suspended in a transverse position to the major and minor psoas muscles. This technic may eliminate pelvic retention, and in many instances it saves the kidney.

MacMyn [14] stated that hydronephrosis and dilatation of the ureters in children does not occur frequently. It may be unsuspected and overlooked, and rapidly cause death. The condition is marked by disorders of urination due to obstruction and to added infection. A valvular obstruction in the posterior urethra is more common than has been previously believed and is the cause of many cases of dilatation of the urinary tract heretofore attributed to other factors. The disease may be associated with other congenital abnormalities, whether in the urinary tract or elsewhere, in the same child.

Tuberculosis.—Dózsa [15] commented on the effect of pregnancy on renal tuberculosis and stated that it presented as serious an outlook to the pregnant woman as does pulmonary tuberculosis. Pregnancy has a deleterious effect on renal tuberculosis. A latent pulmonary process may become active and affect the kidneys; or the process, being latent in the kidneys, may become evident. He does not believe that there may be latent tuberculosis which may be activated by the pregnancy

13. Mezö, Bela v.: Transversopexia renis. Eine neue Methode zur Behandlung der Hydronephrose, Ztschr. f. urol. Chir. **26**:488, 1929.

14. MacMyn, D. J.: On Dilatation of the Ureters and Hydronephrosis in Childhood, Brit. J. Urol. **1**:150, 1929.

15. Dózsa, Eugene: Nierentuberkulose und Gestation, Ztschr. f. urol. Chir. **25**: 310, 1928.

without having given previous symptoms. Clinically, the evidence seems to be that pregnancy may start a renal process just as it does a pulmonary one. Pregnancy may cause an extension of the tuberculous process in the kidney to the cavernous form and cause an added absorption of toxins to those which naturally accompany pregnancy and which are of great importance to mother and child. There are some cases on record in which the condition remained unchanged by pregnancy.

Nephrectomy is indicated if the process is unilateral. Interruption of pregnancy is not sufficient to arrest the process. In bilateral tuberculosis or tuberculosis of the remaining kidney, termination of the pregnancy is indicated, with conservative local treatment. Doza has observed that women on whom nephrectomy has been done go through pregnancy well.

[Compilers' Note.—Pugh [16] recently reviewed the literature on the association of tuberculosis and pregnancy. He found that in 69 per cent of cases in which exacerbation of unilateral tuberculosis occurred during pregnancy, abortion or nephrectomy became necessary immediately. Instead of increasing the necessity for conservative treatment in renal tuberculosis, it seems that pregnancy contraindicates it. Interruption of pregnancy does not stop the tuberculous process, and this procedure is increasingly dangerous in later months. Pugh recommended nephrectomy in these cases. Pregnant women stand the operation well, and it is not more serious than when it is performed in the nongravid state.]

Marx [17] made a study of pregnancy in relationship to tuberculosis of the kidney and the bladder, to isolated tuberculosis of the kidney, to nephrectomy with continuing tuberculosis of the bladder and to tuberculosis in the normal bladder after nephrectomy. He observed that pregnancy aggravated the tuberculosis in each case, and in some instances a secondary infection from the colon bacillus took place. If complications arise, removal of the fetus may be necessary.

Wildbolz [18] has performed 660 nephrectomies for renal tuberculosis, with an operative mortality of from 2.2 to 2.5 per cent. In a series of 140 consecutive nephrectomies for renal tuberculosis he did not have any deaths. In tracing 341 of his patients from ten to twenty-one years after nephrectomy for renal tuberculosis he found that 40 per cent are dead. More than half of them died from tuberculosis of the remaining kidney or from pulmonary tuberculosis. The third most common cause of death was miliary tuberculosis. Fifty-nine per cent of the patients

16. Pugh, W. S.: Tuberculosis of the Kidney in Pregnancy, Ann. Surg. **86**: 591, 1927.

17. Marx, H.: Schwangerschaft und Nierentuberkulose, Beitr. z. klin. d. Tuberk. **71**:625, 1929.

18. Wildbolz, Hans: Renal Tuberculosis, J. Urol. **21**:145, 1929.

are alive, and all but 3 have remained cured of the urogenital tuberculosis. Almost all of his patients who are alive more than ten years after nephrectomy have lost their vesical symptoms and urinate normally.

Merely finding the bacillus of tuberculosis in the urine is not sufficient evidence on which to make a diagnosis of renal tuberculosis. Its presence may be due to so-called tuberculous bacilluria. Bacilli of tuberculosis may pass through the kidney and appear in the urine without eliciting macroscopic changes in tuberculous tissue, and without causing the admixture of pus in the secretion of the kidney. Wildbolz stated that the other microscopic observations are important, and above all the results of the functional tests should help to determine the diagnosis.

The healing of clinically demonstrable caseous renal tuberculosis, if it occurs, is extraordinarily rare. Nephrectomy in cases of bilateral renal tuberculosis is hardly ever justified. Removal of the kidney should be limited to cases of unilateral renal tuberculosis. Wildbolz expressed the belief that greater accuracy in diagnosing renal tuberculosis will eliminate futile and harmful procedures and that nephrectomy will bring permanent cure to many sufferers.

Medlar [19] expressed the belief that excretory bacilluria does not exist unless ulcerative tuberculous lesions are present in the kidney. There may not be any outward manifestations of renal tuberculosis. Infection is usually bilateral and hematogenous. He stated that some tuberculous lesions of the kidney do heal. Medlar agreed with Wildbolz as to the indications for nephrectomy and that if the lesion is bilateral removal of one kidney is contraindicated. Benign forms of renal tuberculosis of man are not of avian origin.

Papin [20] stated that there are three cardinal symptoms of renal tuberculosis, frequency (especially at night), pain during urination and pyuria. There are a few exceptions to this rule, which constitute clinical varieties of renal tuberculosis. He mentioned some of the main types: Pyuria in which there is false albuminuria, few vesical phenomena, but slightly cloudy urine with albuminuria, the latter often misleading the diagnosis. Hematuria often appears in apparently normal persons and is frequently a sign of danger. In hydronephrosis with stricture of the ureter, complete obstruction may result. Tumor occurs, especially in cases of excluded kidneys, such as hydronephrosis and closed pyonephrosis. Chronic nephritis of renal tuberculosis is rare and is the result of closed tuberculosis with sclerosis of the remaining portion of the organ.

19. Medlar, E. M.: Discussion of Renal Tuberculosis, J. Urol. **21**:167, 1929.

20. Papin, E.: Les variétés cliniques de la tuberculose rénale, Paris méd. **69**:328, 1928.

Renal tuberculosis with incontinence rarely occurs; it is more common in children; when it occurs in an adult it is of great diagnostic value.

Dourmashkin [21] has observed that on the affected side in cases of renal tuberculosis the normal pelvic curve of the ureter is obliterated and the catheter goes up to the kidney in an almost straight line. As measured from the tip of the ischial spine, the distance from the catheter to the side of the pelvis is usually greater on the affected side than on the normal side. Dourmashkin concluded that the obliteration of the curve of the pelvis is probably due to a shortening of the ureter as a result of a tuberculous lesion. If the sign is present in conditions other than tuberculosis, ureteropyelographic study should be carried out. The condition has been observed in cases in which lesions are not apparent. Its frequent occurrence in patients with tuberculosis should render it of diagnostic value in doubtful cases or when the tuberculous infection is not suspected.

Hyperplasia.—Pack and Buzzanca,[22] in a study of hydronephrosis and hyperplastic changes in the pelvic mucosa, introduced sterile pebbles into the renal pelvis of experimental animals. From these experiments they concluded that hyperplasia of the transitional epithelium of the renal pelvis is a frequent and early response to the presence of renal stones. Benign villous papillomas of the renal pelvis occasionally follow irritation by renal stones. This occurs later than the more common simple epithelial hyperplasia. Urinary stasis is suggested as one of the factors involved in the formation of tumor within the renal pelvis.

Actinomycosis.—Cumming and Nelson [23] reviewed 9 cases of so-called primary actinomycosis of the kidney and added the data of two cases of their own.

The urinary tract is a relatively common site of actinomycosis, which should be considered a systemic, not a local, disease. The involvement of the kidney or ureter is usually secondary. When the process is apparently confined to the kidney, perinephric abscess is likely to occur. The disease is recognized by finding the typical granules in the urine, in pus from suppurating areas or in the tissues themselves.

The prognosis is usually grave; in secondary involvement the disease is so widespread as to be usually fatal; when primary in the kidney, it is well advanced when treatment is undertaken. Nephrectomy is the best treatment when applicable. Roentgen therapy, potassium iodide and

21. Dourmashkin, R. L.: A Roentgen-Ray Sign in the Diagnosis of Unilateral Renal Tuberculosis, J. Urol. **21**:455, 1929.

22. Pack, G. T., and Buzzanca, Ross: Experimental Production of Epithelial Hyperplasia of the Renal Pelvis, Am. J. Surg. **7**:221, 1929.

23. Cumming, R. E., and Nelson, R. J.: Actinomycosis of the Urinary Tract, Surg. Gynec. Obst. **49**:352, 1929.

copper sulphate are recommended, but are only of accessory value after surgical drainage and removal of the affected organ.

Essential Hematuria.—Warsch,[24] in further elaboration of eliminating cases from the so-called essential hematuria class, cited 3 cases in which the bleeding was explained by subepithelial hematomas in a chronically inflamed pelvic wall. Macroscopic and microscopic examination of the renal parenchyma failed to give any clues to account for the profuse bleeding. These cases illustrate the importance of examining the entire kidney carefully before classifying the case as one of essential hematuria.

URETER

Tumor.—Thomson-Walker [25] reported 3 cases in which nephrectomy was performed for a papillomatous growth in the renal pelvis, and in which at the time the ureter and bladder apparently were not involved. Papilloma of the ureter and bladder developed later, necessitating ureterectomy and treatment by electrocoagulation. Owing to the fact that ureterectomy was performed in these 3 cases within a period of six months, one would be led to believe that papilloma of the renal pelvis was a condition increasing in frequency. In a large proportion of the recorded cases it was noted that the growth spread to the ureter and to the wall of the bladder at the corresponding orifice of the ureter. By performing nephrectomy, the recurrence in ureter and bladder might possibly be prevented. It is evident that examination of the segment of ureter at the time of nephrectomy may be misleading, and that removal of the ureter should be carried out simultaneously with nephrectomy when the condition of the patient permits.

[Compilers' Note.—Recurrence of papilloma in the ureter and bladder frequently occurs. At cystoscopic examination the bladder may appear to be normal. Small papillomatous transplants may be found protruding from or surrounding the ureteral orifice. The papillomatous growths in the renal pelvis, as well as those in the ureter, are more compact than the transplants to the urinary bladder. Most tumors of the renal pelvis are malignant histologically. The transplants to the lower part of the urinary tract, extension to the adjacent tissues and local recurrences make these tumors all clinically malignant. Because of the frequency with which the ureter is involved and the repeated recurrences after nephrectomy, complete nephro-ureterectomy is essential to insure even partial success.]

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24. Warsch, Ninon: Zur Frage der sogenannten "essentiellen Hämaturie" der Niere, Ztschr. f. urol. Chir. **26**:339, 1929.

25. Thomson-Walker, John: Three Cases of Ureterectomy for Papilloma, with Comments, Brit. J. Urol. **1**:141, 1929.

Ureteral Transplantation.—Lisovskaja [26] noted that the mortality statistics of Russian surgeons in ureteral implantations to the rectum for benign lesions, such as fistulas and exstrophy, are about 31 per cent; those of the Mayo Clinic are 20 per cent. He is of the opinion that the latter low percentage in the Mayo Clinic is due to the two-stage operation employed there. In the Russian clinic the method is combined with a prepared autogenous vaccine of the colon bacillus. Two cases in which this method was used progressed satisfactorily. The interval between operations in one case was two months and in the other, six months. Lisovskaja also reported the cases of 3 patients who have remained well ten, twelve and fifteen years, respectively.

[Compilers' Note.—Coffey's recent development of his technic of ureteral implantation based on clinical and experimental work done a number of years ago leads us to hope that this operation will become better standardized and thus be made available to the average urologic surgeon in a relatively short time. From the Mayo Clinic come interesting and encouraging reports of cases in which the patients are thus satisfactorily treated each year, with a definite lowering of the immediate and ultimate mortality. C. H. Mayo was one of the first to use this operation in exstrophy of the bladder. A number of years ago Kidd advocated total resection of the urinary bladder for irresectable neoplasm, the procedure being preceded by implantation of the ureter. The mortality of the operation at that time was prohibitive so far as general adoption of the method was concerned. If the mortality of ureteral implantation can be decreased to a relatively low degree, malignancy of the bladder and probably of the prostate gland can be more radically handled than our present surgical procedures permit. The perseverance of American surgeons, led by Coffey and C. H. Mayo, in overcoming apparently insurmountable technical difficulties and in developing this field of surgery is to be commended.]

Stricture.—Frater and Braasch [27] concluded, from a study of the data from 93 necropsies, that the incidence of inflammatory stricture of the ureter is not so great as recent postmortem studies indicate and that diagnosis of stricture of the ureter by clinical methods now used may be inaccurate. The fact that the infectious origin of stricture of the ureter does occur is generally recognized, but no instance of this type of stricture was observed in their series. The greatest anatomic narrowing in the normal ureter usually occurs within the first 4 cm. from the

26. Lisovskaja, S.: Auf welchem Wege ist die Mortalität bei der Ureterenimplantation in den Darm herabzusetzen? Kuban. naučno-med. **7-8**:40, 1928; abstr., Ztschr. f. urol. Chir. **26**:189, 1929.

27. Frater, Kenneth, and Braasch, W. F.: The Incidence of Stricture of the Ureter, Surg. Gynec. Obst. **48**:390, 1929.

ureteral orifice, which corresponds to the area in which most strictures have been reported. Asymmetry in the two ureters was common; in several cases the caliber of one ureter was 50 per cent greater than that of the other, although both were normal on gross and microscopic examination. Ureteral dilatation, even when it occurs proximal to a portion of the ureter with a comparatively small lumen, does not necessarily indicate stricture. The dilatation in such cases may be atonic and the result of intrinsic cicatricial changes in the wall of the ureter. Stricture is not necessary to the formation of renal or ureteral stone.

Ureteral Anastomosis.—Bump and Crowe [28] examined 6 dogs at varying periods after division and suture of the ureters. The urine had been excluded from the site of repair and the full caliber of the ureter had been maintained. Healing occurred without narrowing or appreciable dilatation of the lumina, with a minimal scar, without change in the renal pelves and without evidence of severe injury to the kidneys.

Ten months after a similar repair of a ruptured ureter in a woman, the ureter was found to be only slightly dilated; the renal pelvis and calices were not appreciably altered.

Reflex.—Gruber [29] experimented with the intravesical portion of the ureter to determine whether there can be reflux of urine into the ureter from the bladder. He concluded that the intravesical portion serves as a true valve, which acts passively, and is not a sphincter dependent on muscle tonus or muscle contraction. In bladders of human beings, cats, dogs, pigs and monkeys, having normal valves, regurgitation does not occur, unless the injection pressures are excessive and the volume of fluid injected exceeds that normally found in the bladder. Cutting away the ureterovesical valve permitted reflux of fluid from the bladder into the ureter in all bladder tests, except in one human bladder with a thick wall. Stretching the mucosa of the bladder by injecting into the bladder excessively large amounts of fluid under high pressure shortens the valves and in many instances renders them incompetent.

[Compilers' Note.—Gruber's composite study of the ureterovesical valve is interesting, especially from the standpoint of comparative anatomy. The fact that the valve in the rabbit differs from that in other animals is important, as the rabbit has been most extensively used in experimental work in this field. That the ureterovesical orifice does become incompetent at times in the face of urinary back-pressure, such as is produced by obstruction of the vesical neck, is attested to by cystograms, which, as Bumpus and others have shown, frequently indicate reflux into the ureters. Such reflux is also noted at times in the cysto-

28. Bump, W. S., and Crowe, S. M.: Uretero-Ureteral Anastomosis, Surg. Gynec. Obst. **48**:346, 1929.

29. Gruber, C. M.: The Uretero-Vesical Valve, J. Urol. **22**:275, 1929.

gram in the presence of a tabetic bladder or when cystography is carried out under caudal or spinal anesthesia. The practice of ureteral meatotomy, which formerly enjoyed such a vogue, is today being more and more abandoned by many urologists on account of subsequent reflux of urine into the ureter and consequent renal infection. This is in accord with Gruber's experimental observations.]

BLADDER

Tumor.—Hunt [30] reported that less than half of the patients with carcinoma of the bladder seen at the Mayo Clinic are amenable to the surgical procedures of excision of the lesion or segmental resection of the bladder.

The surgical excision of lesions affecting one or the other ureter has been difficult, owing to the necessity of properly disposing of the ureter. Extensive segmental resections have been done with consequent involvement of a ureter or ureteral orifice, and the ureter has been reimplanted into the bladder or ligated with a nonabsorbable ligature. A lower mortality has attended ligation of the ureter; nephrectomy on the affected side was required in only about 5 per cent of the cases. Ascending infection has been the cause of about 30 per cent of the immediate mortality when the ureter has been reimplanted into the bladder.

Surgical diathermy has been applicable in lesions of the base of the bladder which have been unsuitable for excision or segmental resection. It is doubtful whether surgical diathermy may be considered as superior to surgical methods in cases in which excision or segmental resection is possible. Hunt stated that a resectable lesion is more successfully treated by surgical excision.

Cystectomy is feasible in only a few instances. Usually when the lesion is unsuitable for excision, resection or surgical diathermy or other physical agents, cystectomy is out of the question because of extravesical extension, remote metastasis, partial or complete ureteral occlusion by the lesion, or the poor condition of the patient. In 1923, 63 cases of cystectomy were reviewed in which the mortality rate was 40 per cent.

Disposition of the ureters has been one of the difficulties of cystectomy. In some cases the operation has been facilitated by preliminary ureterostomy to the loin or inguinal area. In a number of reported cases in which the ureters were transplanted into the sigmoid or rectum simultaneously with cystectomy, there was a high mortality rate. The introduction of ureteral catheters into the ureters and taking them out through the cystectomy wound, or to the surface of the skin, simulta-

30. Hunt, V. C.: Transplantation of the Ureters into the Sigmoid, and Cystectomy for Carcinoma of the Bladder; Report of a Case, Proc. Staff Meet. Mayo Clin. 4:233, 1929.

neous with cystectomy, has been a dangerous procedure because of ascending infection of the kidneys. The high mortality rate in transplantation of the ureters simultaneously with cystectomy does not justify its use as a one-stage operation. In malignant conditions transplantation of ureters is accompanied by more risk than when it is necessary for such conditions as exstrophy of the bladder or irreparable vesicovaginal fistula. Simultaneous transplantation of both ureters is accompanied by greater risk than transplantation of one ureter at a time, with a minimum of two weeks between operations.

When conditions justify cystectomy, it may be done with less risk if the ureters are transplanted into the sigmoid, one at a time, preliminary to cystectomy, and if the bladder is removed several weeks later after good renal function and urinary control have been established with the ureters in the sigmoid, thus confining the cystectomy entirely to an extraperitoneal operation.

Haines [31] stated that a simple uniform classification of tumors of the bladder is needed before any definite and satisfactory procedure of treatment can be attained. Each type of growth should be submitted to one plan of treatment and the results carefully tabulated.

Endovesical fulguration, preceded by roentgen irradiation, is the best treatment for papilloma and early papillary carcinoma when there is no evidence of infiltration and when intractable cystitis is not a complication. In doubtful cases this procedure is worthy of trial. In cases in which definite evidence of infiltration exists, with the tumor favorably situated and not involving ureteral transplantation, and the patient is a good operative risk, resection preceded by roentgen treatment is recommended.

For inoperable tumors, roentgen irradiation followed by intensive diathermy and by cystotomy, may prolong life. Radium destroys the tumor in certain instances, but it does not appreciably lengthen life; it has usually added to the morbidity and hastened death.

Roentgen treatment should be administered before any other treatment, as it does not interfere with subsequent procedures, is harmless when properly applied, and is of some value in many instances.

Hermann,[32] in studying a series of 10 cases of carcinoma of the gastro-intestinal tract in the male, noted that metastasis occurred in the urinary bladder in only 1 instance, whereas it occurred in 6 of 12 cases of Krukenberg's tumor. In these the bladder was involved simultaneously with the tubes and the uterus. The ovaries seem to be a

31. Haines, W. H.: The Treatment of Bladder Tumors, Penn. M. J. **32**: 402, 1929.

32. Hermann, H. B.: Metastatic Tumors of the Urinary Bladder Originating from the Carcinoma of the Gastro-Intestinal Tract, J. Urol. **22**:257, 1929.

determining factor in directing metastatic formation to the pelvic organs. When the ovarian tumor is accompanied by involvement of the pelvic organs operative treatment is not feasible. Symptoms referable to the bladder in cases of Krukenberg's tumor arise from the carcinomatous infiltration of the bladder.

Kaufman [33] stated that hematuria is the most significant sign of carcinoma of the bladder and requires cystoscopy if the patient is more than 50 years of age. The disease is local, has little if any tendency to metastasize but has unusual infiltrative qualities. The type of growth, the site and the structural changes should be ascertained before treatment is instituted. Radical operation, transperitoneal or extraperitoneal, offers the only possibility of cure in cases in which the growth is resectable, with transplantation or high ligation of the ureter when necessary. Radium treatment does not cure in frankly malignant tumors. With or without desiccation, it may be of value in treating small papillary tumors when employed through the cystoscope or by the suprapubic route. Roentgen irradiation is only a palliative measure for pain and occasionally for hemorrhage. Surgical diathermy is an excellent procedure in surgical resection of a tumor and is an efficient agent in checking the growth of the neoplasm in inoperable cases.

A significant symptom of carcinoma of the prostate gland is pain or urinary difficulty, and rectal examination is essential if patients are more than 50 years of age. Metastasis and extension in prostatic carcinoma overshadow the relatively small potential focus of malignancy. Radium is used effectively in limiting the return of the growth, and may be combined with a palliative operation for the relief from urinary obstruction. Permanent suprapubic cystotomy, combined with radium, gives the best general outlook. Radical prostatectomy is limited to only a small group of cases of carcinoma of the prostate gland.

[Compilers' Note.—It would appear that in no field of urologic thought is there so much controversy as that concerning vesical neoplasms. Operation, radium, roentgen rays, diathermy and fulguration have their proponents. During the last few years total cystectomy with ureteral transplantation into the large bowel found an increasing number of advocates. Most urologists are agreed that smaller papillomas should be treated by fulguration. As for the value and possible danger of biopsy, there is dispute but most men favor it. Partial cystectomy when practical and possible of being carried out with reasonable technical ease is still widely practiced, but many surgeons urge that this is done only if tumors are well localized and of a relatively low degree of malignancy. Diathermy or electrocoagulation through an open cystotomy wound for

33. Kaufman, L. R.: Tumors of the Bladder and Prostate with Special Reference to Cancer, S. Clin. N. Amer. 9:701, 1929.

tumors of higher malignancy may be used hopefully. This, however, is not without danger, as some instances of marked sloughing are reported. Ureteral implantation into the bowel, as is being carried out by Coffey and at the Mayo Clinic with an ever decreasing mortality, leads us to hope that eventually this procedure, followed by total cystectomy, will be the solution of the problem of dealing with extensive tumors of the bladder.

Kaufman voices the general opinion in regard to carcinoma of the prostate gland. The advocates of radical prostatectomy are far in the minority, but a few surgeons, such as Young and Wildbolz, report enough success in early cases to make a consideration of the procedure reasonable and worthy of trial in isolated instances, in which the operator discovers malignancy in a gland that has preoperatively been diagnosed as benign.]

Harrison,[34] in reviewing 178 cases of carcinoma of the bladder, concluded that the best results are obtained, in selected cases, from radical operation with resection of the bladder and transplantation of the ureter. When resection was inadvisable and the case was not too advanced or complicated with metastasis, a combination of cystotomy, diathermy and roentgen irradiation resulted in improvement of the condition in 70 per cent of the cases, and of amelioration of symptoms in 90 per cent for varying lengths of time.

Harrison also reviewed 48 cases of carcinoma of the prostate gland. Operation is the procedure of choice if the diagnosis of carcinoma of the gland can be made while it is still confined within the capsule. Radium implants used in conjunction with roentgen rays prolonged life and improved symptoms in more than 70 per cent of the cases.

Bryan [35] reported a case of sarcoma of the bladder. He noted that sarcoma comprises 56.9 per cent of all infantile tumors of the bladder. Sarcoma of the bladder may result as an extension of growth from the surrounding structures and may be of the round cell or spindle cell variety, pedunculated, sessile or infiltrating. It is extremely malignant, as evidenced by metastasis, cellular changes, irregularity in size and shape and staining of the nuclei, abundant nuclei and mitosis. The growths are most often situated about the trigone, but if they are on the wall of the bladder, they bulge or hang like a cluster of grapes.

There are two types of sarcoma: the polypoid tumors, which hang bunchlike, are of rounded elevations of mucous membrane with a more or less constricted base, and the infiltrating, general round cell or spindle

34. Harrison, F. G.: End Results of Carcinoma of Bladder and Prostate Gland, Penn. M. J. **32**:407, 1929.

35. Bryan, R. C.: Sarcoma of the Bladder; Report of a Case, J. Urol. **21**: 695, 1929.

cell sarcoma involving essentially the connective tissue planes of the bladder with wide and symmetric dissemination. Occasionally sarcomas may be pedunculated, but they are usually sessile, with broad bases. Metastasis is common in the retroperitoneal lymph nodes and in the structures about the bladder. Metatasis occurs only by the blood stream and by direct continuity.

The earliest and most reliable symptom is hematuria, which occurs in 62 per cent. The amount of hemorrhage apparently is not indicative of the extent of the tumor.

Bryan referred to Munwes' report of 69 cases of sarcoma of the bladder; 38 patients died soon after operation, and only 3 were considered cured.

Leukoplakia.—Bugbee [36] reported a case of leukoplakia in a diverticulum of the bladder. The diverticulum, lying to the right of the bladder and posterior to it, was resected. The vesical orifice was thoroughly dilated. The mucous membrane of the bladder was normal except for moderate congestion. Pathologic examination revealed leukoplakia-like areas in the denser portion of the diverticulum.

Leukoplakia is almost always associated with long-continued, chronic infection; it progresses slowly, and the only cure is by excision. It is apparently a necessary preliminary to epidermoid or squamous cell carcinoma. Bugbee stated that the possibility of its occurrence in a diverticulum of the bladder is a strong argument for the early removal of a diverticulum by resection.

Exstrophy.—Turner [37] reported 17 cases of transplantation of ureters into the bowel for congenital defects, with 4 deaths (23.5 per cent) directly due to the operation. One patient died more than three years after operation and another more than two years, both having been in good health during the interim. Of the remaining 11 patients, 1 is included twice, which leaves 10 patients alive and well at periods varying from fifteen years to seven months after operation. In most cases the operation was performed in two stages, a total of twenty-eight separate operations, making the mortality 14.3 per cent. Considering that there were twenty-nine separate transplantations of the ureters, with four deaths, the mortality is 13.8 per cent. In a series of 60 cases in the Mayo Clinic the mortality was 13.33 per cent. The cause of death in 3 of Turner's cases was peritonitis. The fourth death occurred in a child aged 1 year and 4 months from general septic dermatitis.

36. Bugbee, H. G.: Leukoplakia in a Diverticulum of the Bladder, J. Urol. **21**:395, 1929.

37. Turner, G. G.: The Treatment of Congenital Defects of the Bladder and Urethra by Implantation of the Ureters into the Bowel; with a Record of Seventeen Personal Cases, Brit. J. Surg. **17**:114, 1929.

Fatalities usually have occurred either when both ureters were transplanted at one time, or after the transplantation of the second ureter in the divided operation. In general, Turner's operative technic is similar to that employed by C. H. Mayo and by Coffey.

The general health of the 10 surviving patients was found to be practically normal. It sometimes takes months or even as long as two years before patients become accustomed to the altered state. Meanwhile, they are acquiring complete rectal toleration, and the kidneys are presumably accommodating themselves to the element of constant mild infection. The time required for the lower part of the bowel to become accustomed to the presence of urine and to the unusual amount of fluid is variable. The younger the patient, the less the control at first. After the second stage of the operation, toleration at night comes rather quickly. Immediately after the operation and for the first day or two, the urine seems to flow constantly from the anus. Owing to the fact that the presence of a foreign body in the anus is greatly resented, Turner does not always persist in keeping a catheter in the bowel. Once toleration has been acquired, most patients can retain urine for several hours during the day, and nearly all night, without discomfort. The average length of time was ascertained to be three hours; the longest period was four and a half hours. Most of the patients get up once at night, sometimes two or three times.

None of the patients of this series showed definite evidence of gross renal insufficiency. That some degree of ascending renal infection develops is borne out by the fact that in two postmortem investigations there was definite, gross evidence of its existence, although neither patient suffered from symptoms indicating its presence. Among the 10 living patients there are 3 who at seven years, three years and three months, and eight months after operation had not suffered from symptoms of renal infection. A moderate degree of renal infection apparently is not inconsistent with average good health. Turner's patients are in good average health and able to withstand the trials of their ordinary environment. Several of them successfully underwent operations under general anesthesia without unusual symptoms. One patient was not more than ordinarily disturbed by pregnancy and lactation. The fact that both patients who died after operations subsequent to the transplantations showed acute renal infection added to the gross and long-standing changes, is not, in his opinion, evidence that they were suffering in that way before their fatal illness.

Rupture.—Sisk and Wear [38] reported a case of spontaneous rupture of the urinary bladder of the extraperitoneal type. There are two types

38. Sisk, I. R., and Wear, J. B.: Spontaneous Rupture of the Urinary Bladder, J. Urol. **21**:517, 1929.

of spontaneous rupture of the bladder, the extraperitoneal and the intraperitoneal, depending on the site of the perforation. Extraperitoneal rupture is less common and less grave than the intraperitoneal type.

The etiology of spontaneous rupture of the bladder depends on some obstruction to urination or interference with the nerve supply of the bladder, resulting in distention of the bladder. The secondary factor is usually pathologic change in the wall of the bladder.

Symptoms and diagnosis depend on whether the rupture is intraperitoneal or extraperitoneal. In either type, the history of previous urinary difficulty and the finding of some type of obstruction is significant. In the extraperitoneal cases there is pain and swelling above the pubis, which soon results in the formation of pus. Because of the seriousness of the intraperitoneal type, early diagnosis is important. At the time of rupture, the patient usually experiences sharp abdominal pain and some shock. Normally there is marked desire and difficulty of urination.

The treatment in both types of spontaneous rupture of the bladder is immediate operation. In extraperitoneal rupture, if the condition of the patient permits, good results are obtained by the introduction of a suprapubic tube and relief from the direct cause. In the intraperitoneal type the abdomen should be opened and drained, and the opening in the bladder closed in layers, with adequate drainage provided by an indwelling urethral catheter or a suprapubic tube.

(To be concluded)